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FORM PTO-1390 (REV. 1-98) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: 446.001

U.S. APPLICATION NO. (If known, see 37 CFR 1.5): 09/786880

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/EP99/07376	September 13, 1999	September 11, 1998

TITLE OF INVENTION: ESSENTIAL GENES FROM C. ALBICANS AND A METHOD FOR SCREENING ANTIMYCOTIC SUBSTANCES USING SAID GENES.

APPLICANT(S) FOR DO/EO/US: LALANNE et al

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.
3. [X] This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. [ ] A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   - a. [X] is transmitted herewith (required only if not transmitted by the International Bureau). in English
   - b. [ ] has been transmitted by the International Bureau.
   - c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US).
6. [ ] A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. [ ] Amendments to the claims of the International Aplication under PCT Article 19 (35 U.S.C. 371(c)(3))
   - a. [ ] are transmitted herewith (required only if not transmitted by the International Bureau).
   - b. [ ] have been transmitted by the International Bureau.
   - c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   - d. [ ] have not been made and will not be made.
8. [ ] A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).
9. [X] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). (UNEXECUTED)
10. [ ] A translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern document(s) or information included:

11. [ ] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. [ ] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. [ ] A FIRST preliminary amendment.
    [ ] A SECOND or SUBSEQUENT preliminary amendment.
14. [ ] A substitute specification.
15. [ ] A change of power of attorney and/or address letter.
16. [X] Other items or information: PCT/RO/101; PCT/IB/306; PCT/IPEA/401; International Preliminary Examination Report; Papers to the International Depositary Authority (8 pages in English; 9 pages in French) Drawings (9 sheets); Sequence Listing (83 sheets)

JC02 Rec'd PCT/PTO 08 MAR 2001

U.S. APPLICATION NO. (if known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
09/786880	PCT/EP99/07376	446.001

				CALCULATIONS	PTO USE ONLY
17. [X] The following fees are submitted:					
BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):				$1000.00	
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO $1070.00					
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO $930.00					
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO $790.00					
International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) $720.00					
International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) $98.00					
ENTER APPROPRIATE BASIC FEE AMOUNT =				$1000.00	
Surcharge of $130.00 for furnishing the oath or declaration later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(e)).				$	
CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	$ 414.00	
Total claims	43 -20 =	23	x18	$	
Independent claims	10 -3 =	7	x80	$ 560.00	
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ $270.00	$	
TOTAL OF ABOVE CALCULATIONS =				$	
Reduction of 1/2 for filing by small entity, if applicable. A Small Entity Statement must also be filed (Note 37 CFR 1.9, 1.27, 1.28). +				$	
SUBTOTAL =				$1974.00	
Processing fee of $130.00 for furnishing the English translation later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(f)).				$	
TOTAL NATIONAL FEE =				$1974.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). $40.00 per property +				$	
TOTAL FEES ENCLOSED =				$1974.00	
				Amount to be refunded:	$
				charged:	$

a. [X] A check in the amount of $1974.00 to cover the above fees is enclosed.

b. [ ] Please charge my Deposit Account No. ____________ in the amount of $ __________ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. [X] The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 02-2275 A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Charles A. Muserlian
Bierman, Muserlian and Lucas
600 Third Avenue
New York, NY 10016

20311
PATENT TRADEMARK OFFICE

SIGNATURE

Charles A. Muserlian
NAME

19,683
REGISTRATION NUMBER

09/786880

446.001 Rec'd PCT/PTO 08 AUG 2001

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

OIPE
AUG 06 2001
JC103
PATENT & TRADEMARK OFFICE

In re Application of:
JEAN-LOUIS LALANNE et al
Serial No.: 09/786,880
Filed: March 8, 2001
For: ESSENTIAL GENES...SAID GENES

600 Third Avenue
New York N.Y. 10016
August 6, 2001

AMENDMENT

Asst. Commissioner for Patents
Washington, D.C. 20231

Sir:

Please amend this application as follows:

IN THE SPECIFICATION:

Page 3, rewrite the second paragraph as follows:

--According to another aspect, the present invention concerns a polynucleotide having the sequence as depicted in SEQ ID No. 2, SEQ ID No. 5, SEQ ID No. 8, SEQ ID No. 10, SEQ ID No. 13. SEQ ID No. 15, SEQ ID No.17, SEQ ID No. 20, preferably SEQ ID No. 2, SEQ ID No. 5, SEQ ID No. 8, SEQ ID No. 13, SEQ ID No. 14 or SEQ ID No. 17, homologs thereof and functional fragments thereof.--

Replace pages 32 to 37 and 39 with the replacement pages filed herewith.

08/13/2001 KKAYPASH 00000029 09786880

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IN THE CLAIMS:

Claim 1 (amended) A polynucleotide having the sequence as depicted in the sequence selected from the group consisting of SEQ ID No. 2, SEQ ID No. 5, SEQ ID No. 8, SEQ ID No. 10, SEQ ID No. 13,

[redacted]

SEQ ID No. 15, SEQ ID No. 17 or SEQ ID No. 20, homologs thereof and functional fragments thereof.

REMARKS

The present amendment is being filed in order to amend the specification in accordance with the floppy disk with the sequences filed herewith. The floppy disk was not generated in the same way the sequences were generated at the time of filing the PCT application. For the genes encoding the protein, the PCT provides the "subsequences". Therefore, a shift had to occur and the diskette filed herewith contains the sequences generated using the proper software. The following table gives the correspondence between the sequences and the specification and claims have been amended accordingly.

SEQ ID No. in PCT Publication	SEQ No. in Electronic Sequence Listings	SEQ ID No. in PCT Publication	SEQ No. in Electronic Sequence Listings
1	1	10	15
2	2	11	17
3	4	12	19
4	5	13	20
5	7	14	22
6	8	15	23
7	10	16	24
8	12	17	25
9	13		

Applicants are submitting herewith a hard copy of the sequence listing as well as the computer readable form (CRF) of the sequence listing. The contents of the paper sequence listing and the computer readable form are the same and where applicable, include no new matter as required by 37 CFR 1.821(e). 1.821(f), 1.821(g), 1.825(b) or 1.825(d).

Respectfully submitted,
Bierman, Muserlian and Lucas

By: ______________________
Charles A. Muserlian #19,683
Attorney for Applicants
Tel.# (212) 661-8000

CAM:ds
Enclosures

MARKED UP VERSION OF PAGE 3

According to another embodiment of the method of the invention said functional similar genes are essential genes from Candida Spp., preferably Candida albicans, or from Aspergillus Spp., preferably from Aspergillus fumigatus.

According to another aspect, the present invention concerns a polynucleotide having the sequence as depicted in SEQ ID No.2, SEQ ID No.~~4~~5, SEQ ID No.~~6~~8, SEQ ID No.~~7~~10, SEQ ID No.~~9~~13, SEQ ID No.~~10~~15, SEQ ID No.~~11~~17 or SEQ ID No.~~13~~20, preferably SEQ ID No.2, SEQ ID No.~~4~~5, SEQ ID No.~~6~~8, SEQ ID No.~~9~~13, SEQ ID No.~~10~~15 or SEQ ID No.~~11~~17, homologs thereof and functional fragments thereof.

According to another aspect, the present invention concerns a gene which is CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, preferably CaOR110, CaMR212, CaNL256, CaBR102 or CaIR012, or a functionally similar gene or a functional fragment thereof.

According to this embodiment, the functionally similar gene or homologous polynucleotide has a sequence identity, at the nucleotide level, with CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, respectively, of at least 50%, preferably of at least 60%, and most preferably of at least 70%. A functional fragment is a polynucleotide fragment that will retain the functionality of the starting product (nucleotide or gene). One example is the CaOR110 splice variant (which is also homologous to the original gene, with about 90% identity).

According to another embodiment, the functionally similar gene has a sequence identity, at the amino-acid level, with CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, respectively, encoded protein(s) of at least 40%, preferably of at least 50%, more preferably of at least 60% and most preferably of at least 70%.

Example 2 : CaBR102

The Internet site of Stanford (http://candida.stanford.edu/) give access to preliminary sequences of the genome of C. albicans. One of these sequences has homology with the YBR102 gene of S.cerevisiae. Two oligonucleotides were selected in this sequence (5'-AGTATTCAATTGGGTATTCC-3' and 5'-CCGGCATCATCAGTAACTCC-3') in order to amplified the corresponding fragment of C. albicans. After cloning, we obtained a sequence of 647 bp (SEQ ID NO:~~3~~4). The deduced protein was compared with the one of YNL102, evidencing 35% similarity and 26% identity (fig.2). This fragment was amplified using Pfu polymerase (Stratagene). The PCR product was purified (High Pure PCR Product Purification Kit, Boehringer Mannheim) and used as a probe for screening a C. albicans genomic DNA library. The latter was prepared by partial digestion of C. albicans genomic DNA with SauIIIA and cloning into the YEP-24TRP1 vector at the BamHI restriction site. 40,000 clones of the library were then spread at a density of 2000 clones per dish. Each dish was covered by a nitrocellulose filter (Membrane Hybond N^+, Amersham) which was then successively treated with : 1.5 M NaCl/0.5 M NaOH, 5 minutes; 1.5 M NaCl/0.5 M Tris-HCl pH 7.2/1 mM EDTA, 3 minutes, twice; DNA was crosslinked to the filters (Amersham Life Science, ultra violet crosslinker). The probe (100 ng) was labelled with ^{32}P using the RediPrime kit and dCTP (Amersham Life Science). The filters were hybridized in a buffer containing 30% formamide, 5 x SSC, 5% Denhart's solution, 1% SDS, 100 μg /ml salmon sperm DNA and a probe concentration of 10^6 cpm/ml at 42°C for 16 h. The membranes were then washed three times at room temperature in 2 x SSC/0.1% SDS for 5 minutes each and three times in 1 x SSC/0.1% SDS at 60°C for 20 minutes each. the filters were then exposed overnight to an X-ray

film. The colonies corresponding to the positives clones were isolated and screened a second time by the same procedure. Two positives clones were finally obtained, which were sequenced on an ABI377 apparatus. the sequences were compiled using ABI software and then analysed using the GCG software package. The nucleotide sequences of these two clones were identical and contained the complete coding sequence corresponding to the probe used, this gene was called CaBR102, whose sequence is represented in SEQ ID No:4. The translation of this nucleotide sequence was examined, account was taken of the fact that in C. albicans the CTG codon is translated to serine (there are 3 CTG codons in CaBR102). The deduced protein has 24% identity to S. cerevisiae gene YBR102.

Example 3 : CaIR012

Chromosomal DNA from the C. albicans strain Caf2-1 was isolated using Yeast Cell Lysis prep Kit and Genome DNA Kit from BIO101. A 343 bp fragment from C. albicans genomic DNA (SEQ ID NO:5) was amplified with the oligonucleotide primers CaYIR012-5' (5'-GACGTCGTAGACGATACTCAAGAAG-3') and CaYIR012-3' (5'-CTGCAGTAAACCCTCCAGATATAACAG-3') by PowerScript DNA polymerase (PAN Systems GmbH) using the hot start technique. The PCR product was purified from the agarose gel and labeled with fluorescein (Gene image random prime labelling module, Amersham Life Science) according to the manufacturer's instructions. Plasmid DNA from E.coli was isolated using Qiagen columns as recommended by the manufacturer. Screening the λZAPII C. albicans cDNA library was performed following the manufacturer's instructions (Stratagene Ltd.). Nylon filters (Schleicher&Schuell) were lifted from LB-plates (150 mm) with 15000 pfu/plate, denatured 5 min in 1.5M NaCL, 0.5M NaOH, neutralized 3 min in 1.5M NaCl, 0.5M Tris-HCl pH8.0, washed 2 min in 0.2 M Tris-HCl pH 7.5, 2xSSC and DNA was

crosslinked to the filters (Stratagene UV crosslinker). The filters were prehybridized 4 h at 60 °C and hybridized with the fluorescein-labeled DNA probe overnight at 60 °C. Detection was performed with Anti-fluorescein AP conjugate (Signal amplification module for the FluorImager, Amersham LIFE SCIENCE) and analysed after 20 h with a Fluorimager (Storm 860, Molecular Dynamics). Positive plaques were picked and incubated with 0.5 ml SM-buffer (100mM NaCl, 8 mM $MgSO_4$, 50 mM Tris-HCl pH7.5, 0,01% gelatin). The selected clones were diluted, titered with host cells XL1-Blue and screened and purified a second time by the same procedure. Finally, the pBluescript SK(-) phagemid containing the DNA insert of interest was rescued by the ExAssist Helper Phage system according to the Stratagene protocol. From a total of 75000 screened plaques, 3 positive clones were identified. pBluescript SK (-) phagemid DNA was isolated, sequenced with T3 and T7 primers and the sequences were extended with custom-synthesized oligonucleotide primers. Nucleotide sequence analyses were performed with the Gene Data software package (Gene Data AG, Basel Switzerland). Similarity searches with the Swissprot database were conducted with the BLAST program (Gish, Warren and David J. States (1993). Identification of protein coding regions by database similarity search. Nat. Genet. 3:266-72.). One of these three clones turned out to contain the complete coding sequence corresponding to the probe used; this gene was called CaIR1012, whose sequence is represented in SEQ ID NO:~~6~~8.

<u>Example 4: CaJL039</u>

The CaJL039 sequence is depicted in SEQ ID No 7.

The CaJL039 gene was cloned based on gene fragment data issued from the public Stanford *Candida albicans* sequencing database.

(a) A fragment that showed homology to *Saccharomyces cerevisiae* YJL039c was identified, the sequence of which is given in SEQ ID No ~~8~~12.

Using the procedure disclosed in example 3 with the oligonucleotide primer pair (Ca039s: TAG CTC AAC CTA CCA CCA ATC /Ca039r: ATC ACA AGA CTG TCA ATG TAA AT), a short PCR fragment (234 base pairs long) was amplified for screening a Candida albicans cDNA lambda ZAP II library (gift of Alistair Brown, Aberdeen).

Three positive clones of the 3' coding region were obtained.(# 21t7, 11t3, 21t3).

(b) 3'- and 5'- extension of the internal fragment using the primer walking method

The Sanglard genomic Candida DNA library with the YEp24 vector backbone was used for further amplification of 3'- and 5'-coding sequences. Amplification was carried out by using the following vector-specific oligonucleotide primers and CaJL039 fragment-specific primers:

cggaattcctatcgactacgcgatcatgg: YEp24for (vector specific)

gcgaattccgatataggcgccagcaac: YEp24ba (vector specific)

caattgctttgactcgggtgttattaagt: Ca039-51 (CaJL039: 5'fishing)

tcttggcacaacttgataagaatctgt: Ca039-52 (")

taggtgtacgcgaaagccaagtagaac:Ca039-53 (")

ttgttaatcgtacacctaaggtgttgac: Ca039-31 (CaJL039: 3'fishing)

ttgcagattgatgctagcaatgtatttg: Ca039-32 (")

Using the technique of primer walking, the complete 5'-sequence could be amplified (clone 14b-1-1 and clone 17b-3-4).

The missing 3'-sequence was available from GTC PathoGenome Release 5.0, contig #2830.

An interacting protein (C82, component for RNA polymerase III in yeast) has been identified.

Example 5: CaOR110

5.1. CaOR110

The CaOR110 sequence is depicted in SEQ ID No ~~9~~ 13.

CaOR110 was cloned based on gene fragment data issued from the public Stanford *Candida albicans* sequencing database.

(a) A small ScOR110-homologous fragment was used in a hybridization experiment to identify CaOR110 clones in a *Candida Albicans* lambda ZAPII cDNA library (from Alistair Brown). Alignement of Candida Albicans CaOR110 sequence with the fragment used for hybridization is given in figure 3. The homologous fragment sequence is given in SEQ ID No. ~~17~~ 25.

(b) 3´- and 5´- Extension of the internal fragment:

The Sanglard genomic Candida DNA library (received from RMV) in the YEP24 vector backbone was used for the amplification of 3´- and 5´- coding and non-coding sequences. This amplification was done by using the vector-specific oligos (directional towards the insert) and CaOR110 fragment-specific oligos (directional towards the vector flanking sequences) described below:

cggaattcctatcgactacgcgatcatgg : YEP24for
gcgaattccgatataggcgccagcaac : YEP24ba
cgggatccggtaaccaattggatctataaccgtg : 110-ba-150
gcggatcctggtgcccttggtggtgaatg : CaYOR110A
gcggatccctcacaatatgacgattgaaact : CaYOR110B
ggcgtcgactcaggcgccagttttacgtacttcaaattcatc : CaYOR110C
tgtgaattcttgacacagggtga : CaYOR110D
caaaccttcagcacaactcca : CaYOR110E

The finaly assembled sequence that included also 3´- and 5´- non-coding sequences was verified by sequencing. The coding region was subcloned into the p414RSGALL-vector.

The map is depicted in Fig. 4.

The homologous yeast ORF (YOR110w) has been described as the transcription factor subunit TFC7 interacting with TFC1 in the TFIIIC polymerase complex (Manaud et al., 1998, Mol. Cell. Biol. 18; 3191-3200).

5.2. CaOR110 splice variant

For CaOR110, an additional splice variant was identified. The clones for the splice variant of CaOR110 were obtained from a Candida albicans cDNA library.

The sequence is depicted in SEQ ID No. ~~10~~ 15.

The splice variant uses the donor site "gtacgt" at position 907 of the original CaOR110 sequence. Acceptor site is at 1047. The map is disclosed in Fig. 5.

The alignement of the original CaOR110 and the splice variant is given in fig. 6.

Example 6 : CaMR212

The CaMR212 sequence is depicted in SEQ ID No. ~~11~~ 17.

(a) CaMR212 was cloned based on gene fragment data from the public Standford *Candida albicans* sequencing database.

The sequence of a fragment showing homology (Blast search) to the *Saccharomyces cerevisiae* gene YMR212c is given in SEQ ID ~~12~~ 18.

Based on these data, the following oligos were designed that allow amplification of this fragment (490 bp-fragment) from genomic *Candida albicans* DNA.

Oligos:

CaYMR212for: 5´- cacctgtgaacaacccaccatc-3´

CaYMR212back: 5´- gaatatccttttaactcaagag -3´

(b) 3´- and 5´- extension of this internal fragment from CaMR212

For this purpose, genomic Candida DNA libraries from Dominique Sanglard (received from RMV) were used. The YEp24 backbone of this library was used to amplify the 3´- and 5´- coding and non coding sequences with PCR. This was done

by microscope analysis of YMR212-GFP fusion proteins and by biochemical analysis of YMR212-GST fusion proteins).

Example 7 : CaDR325

The CaDR325 sequence is given at SEQ ID ~~13~~ 20.

CaDR325 was cloned based on gene fragment data from the public Stanford *Candida albicans* sequencing database.

(a) 3 fragments that showed homology to *Saccharomyces cerevisiae* YDR325 were identified, the sequences of which are disclosed in SEQ ID ~~14~~ 22, ~~15~~ 23 and ~~16~~ 24.

Based on these data, the following oligos were designed that allowed the verification of the database sequences and the amplification of an approx. 2200 bp internal CaDR325 fragment from genomic DNA:

cgagcatctacttgttcaaccac: hybCaYDR325ba Oligo

gaatctctggctcgctc: 325-juls Oligo

gaccgagatacacgagaat: 325-julr Oligo

ggttaaatgatcgtgatgaat: Ca325r Oligo

caacctcactgacaaatactt: Ca325s Oligo

The finally subcloned 2200 bp internal fragment was amplified by the combination hybCaYDR325ba + 325-julr oligos.

(c) 3´- and 5´- Extension of the internal fragment:

The Sanglard genomic Candida DNA library (received from RMV) in the YEP24 vector backbone was used for the amplification of 3´- and 5´- coding and non-coding sequences. This was done by using the following vector-specific oligos (directional towards the insert) and CaDR325 2200 bp fragment-specific oligos (directional towards the vector flanking sequences):

cggaattcctatcgactacgcgatcatgg : YEP24for (vector specific)

gcgaattccgatataggcgccagcaac : YEP24ba (vector specific)

acgcttccaatgtattattctcg : Oligo 1-10-A back

Example 2 : CaBR102

The Internet site of Stanford (http://candida.stanford.edu/) give access to preliminary sequences of the genome of C. albicans. One of these sequences has homology with the YBR102 gene of S.cerevisiae. Two oligonucleotides were selected in this sequence (5'-AGTATTCAATTGGGTATTCC-3' and 5'-CCGGCATCATCAGTAACTCC-3') in order to amplified the corresponding fragment of C. albicans. After cloning, we obtained a sequence of 647 bp (SEQ ID NO:4). The deduced protein was compared with the one of YNL102, evidencing 35% similarity and 26% identity (fig.2). This fragment was amplified using Pfu polymerase (Stratagene). The PCR product was purified (High Pure PCR Product Purification Kit, Boehringer Mannheim) and used as a probe for screening a C. albicans genomic DNA library. The latter was prepared by partial digestion of C. albicans genomic DNA with SauIIIA and cloning into the YEP-24TRP1 vector at the BamHI restriction site. 40,000 clones of the library were then spread at a density of 2000 clones per dish. Each dish was covered by a nitrocellulose filter (Membrane Hybond N^{+}, Amersham) which was then successively treated with : 1.5 M NaCl/0.5 M NaOH, 5 minutes; 1.5 M NaCl/0.5 M Tris-HCl pH 7.2/1 mM EDTA, 3 minutes, twice; DNA was crosslinked to the filters (Amersham Life Science, ultra violet crosslinker). The probe (100 ng) was labelled with ^{32}P using the RediPrime kit and dCTP (Amersham Life Science). The filters were hybridized in a buffer containing 30% formamide, 5 x SSC, 5% Denhart's solution, 1% SDS, 100 μg /ml salmon sperm DNA and a probe concentration of 10^6 cpm/ml at 42°C for 16 h. The membranes were then washed three times at room temperature in 2 x SSC/0.1% SDS for 5 minutes each and three times in 1 x SSC/0.1% SDS at 60°C for 20 minutes each. the filters were then exposed overnight to an X-ray

film. The colonies corresponding to the positives clones were isolated and screened a second time by the same procedure. Two positives clones were finally obtained, which were sequenced on an ABI377 apparatus. the sequences were compiled using ABI software and then analysed using the GCG software package. The nucleotide sequences of these two clones were identical and contained the complete coding sequence corresponding to the probe used, this gene was called CaBR102, whose sequence is represented in SEQ ID No:4. The translation of this nucleotide sequence was examined, account was taken of the fact that in C. albicans the CTG codon is translated to serine (there are 3 CTG codons in CaBR102). The deduced protein has 24% identity to S. cerevisiae gene YBR102.

Example 3 : CaIR012

Chromosomal DNA from the C. albicans strain Caf2-1 was isolated using Yeast Cell Lysis prep Kit and Genome DNA Kit from BIO101. A 343 bp fragment from C. albicans genomic DNA (SEQ ID NO:7) was amplified with the oligonucleotide primers CaYIR012-5' (5'-GACGTCGTAGACGATACTCAAGAAG-3') and CaYIR012-3' (5'-CTGCAGTAAACCCTCCAGATATAACAG-3') by PowerScript DNA polymerase (PAN Systems GmbH) using the hot start technique. The PCR product was purified from the agarose gel and labeled with fluorescein (Gene image random prime labelling module, Amersham Life Science) according to the manufacturer's instructions. Plasmid DNA from E.coli was isolated using Qiagen columns as recommended by the manufacturer. Screening the λZAPII C. albicans cDNA library was performed following the manufacturer's instructions (Stratagene Ltd.). Nylon filters (Schleicher&Schuell) were lifted from LB-plates (150 mm) with 15000 pfu/plate, denatured 5 min in 1.5M NaCL, 0.5M NaOH, neutralized 3 min in 1.5M NaCl, 0.5M Tris-HCl pH8.0, washed 2 min in 0.2 M Tris-HCl pH 7.5, 2xSSC and DNA was

crosslinked to the filters (Stratagene UV crosslinker). The filters were prehybridized 4 h at 60 °C and hybridized with the fluorescein-labeled DNA probe overnight at 60 °C. Detection was performed with Anti-fluorescein AP conjugate (Signal amplification module for the FluorImager, Amersham LIFE SCIENCE) and analysed after 20 h with a Fluorimager (Storm 860, Molecular Dynamics). Positive plaques were picked and incubated with 0.5 ml SM-buffer (100mM NaCl, 8 mM $MgSO_4$, 50 mM Tris-HCl pH7.5, 0,01% gelatin). The selected clones were diluted, titered with host cells XL1-Blue and screened and purified a second time by the same procedure. Finally, the pBluescript SK(-) phagemid containing the DNA insert of interest was rescued by the ExAssist Helper Phage system according to the Stratagene protocol. From a total of 75000 screened plaques, 3 positive clones were identified. pBluescript SK (-) phagemid DNA was isolated, sequenced with T3 and T7 primers and the sequences were extended with custom-synthesized oligonucleotide primers. Nucleotide sequence analyses were performed with the Gene Data software package (Gene Data AG, Basel Switzerland). Similarity searches with the Swissprot database were conducted with the BLAST program (Gish, Warren and David J. States (1993). Identification of protein coding regions by database similarity search. Nat. Genet. 3:266-72.). One of these three clones turned out to contain the complete coding sequence corresponding to the probe used; this gene was called CaIR1012, whose sequence is represented in SEQ ID NO:8.

Example 4: CaJL039

The CaJL039 sequence is depicted in SEQ ID No 7.

The CaJL039 gene was cloned based on gene fragment data issued from the public Stanford *Candida albicans* sequencing database.

(a) A fragment that showed homology to *Saccharomyces cerevisiae* YJL039c was identified, the sequence of which is given in SEQ ID No 12.

Using the procedure disclosed in example 3 with the oligonucleotide primer pair (Ca039s: TAG CTC AAC CTA CCA CCA ATC /Ca039r: ATC ACA AGA CTG TCA ATG TAA AT), a short PCR fragment (234 base pairs long) was amplified for screening a Candida albicans cDNA lambda ZAP II library (gift of Alistair Brown, Aberdeen).

Three positive clones of the 3' coding region were obtained. (# 21t7, 11t3, 21t3).

(b) 3'- and 5'- extension of the internal fragment using the primer walking method

The Sanglard genomic Candida DNA library with the YEp24 vector backbone was used for further amplification of 3'- and 5'-coding sequences. Amplification was carried out by using the following vector-specific oligonucleotide primers and CaJL039 fragment-specific primers:

cggaattcctatcgactacgcgatcatgg: YEp24for (vector specific)

gcgaattccgatataggcgccagcaac: YEp24ba (vector specific)

caattgctttgactcgggtgttattaagt: Ca039-51 (CaJL039: 5'fishing)

tcttggcacaacttgataagaatctgt: Ca039-52 (`)

taggtgtacgcgaaagccaagtagaac:Ca039-53 (`)

ttgttaatcgtacacctaaggtgttgac: Ca039-31 (CaJL039: 3'fishing)

ttgcagattgatgctagcaatgtatttg: Ca039-32 (`)

Using the technique of primer walking, the complete 5'-sequence could be amplified (clone 14b-1-1 and clone 17b-3-4).

The missing 3'-sequence was available from GTC PathoGenome Release 5.0, contig #2830.

[redacted]

An interacting protein (C82, component for RNA polymerase III in yeast) has been identified.

Example 5: CaOR110

5.1. CaOR110

The CaOR110 sequence is depicted in SEQ ID No 13.

CaOR110 was cloned based on gene fragment data issued from the public Stanford *Candida albicans* sequencing database.

(a) A small ScOR110-homologous fragment was used in a hybridization experiment to identify CaOR110 clones in a *Candida Albicans* lambda ZAPII cDNA library (from Alistair Brown). Alignement of Candida Albicans CaOR110 sequence with the fragment used for hybridization is given in figure 3. The homologous fragment sequence is given in SEQ ID No. 25.

(b) 3´- and 5´- Extension of the internal fragment:

The Sanglard genomic Candida DNA library (received from RMV) in the YEP24 vector backbone was used for the amplification of 3´- and 5´- coding and non-coding sequences. This amplification was done by using the vector-specific oligos (directional towards the insert) and CaOR110 fragment-specific oligos (directional towards the vector flanking sequences) described below:

cggaattcctatcgactacgcgatcatgg : YEP24for

gcgaattccgatataggcgccagcaac : YEP24ba

cgggatccggtaaccaattggatctataaccgtg : 110-ba-150

gcggatcctggtgcccttggtggtgaatg : CaYOR110A

gcggatccctcacaatatgacgattgaaact : CaYOR110B

ggcgtcgactcaggcgccagttttacgtacttcaaattcatc : CaYOR110C

tgtgaattcttgacacagggtga : CaYOR110D

caaaccttcagcacaactcca : CaYOR110E;

The finaly assembled sequence that included also 3´- and 5´- non-coding sequences was verified by sequencing. The coding region was subcloned into the p414RSGALL-vector.

The map is depicted in Fig. 4.

The homologous yeast ORF (YOR110w) has been described as the transcription factor subunit TFC7 interacting with TFC1 in the TFIIIC polymerase complex (Manaud et al., 1998, Mol. Cell. Biol. 18; 3191-3200).

5.2. CaOR110 splice variant

For CaOR110, an additional splice variant was identified. The clones for the splice variant of CaOR110 were obtained from a Candida albicans cDNA library.

The sequence is depicted in SEQ ID No.15.

The splice variant uses the donor site "gtacgt" at position 907 of the original CaOR110 sequence. Acceptor site is at 1047. The map is disclosed in Fig. 5.

The alignement of the original CaOR110 and the splice variant is given in fig. 6.

Example 6 : CaMR212

The CaMR212 sequence is depicted in SEQ ID No.17.

(a)CaMR212 was cloned based on gene fragment data from the public Standford *Candida albicans* sequencing database.

The sequence of a fragment showing homology (Blast search) to the *Saccharomyces cerevisiae* gene YMR212c is given in SEQ ID . 19.

Based on these data, the following oligos were designed that allow amplification of this fragment (490 bp-fragment) from genomic *Candida albicans* DNA.

Oligos:

CaYMR212for: 5´- cacctgtgaacaacccaccatc-3´

CaYMR212back: 5´- gaatatccttttaactcaagag -3´

(b) 3´- and 5´- extension of this internal fragment from CaMR212

For this purpose, genomic Candida DNA libraries from Dominique Sanglard (received from RMV) were used. The YEp24 backbone of this library was used to amplify the 3´- and 5´- coding and non coding sequences with PCR. This was done

by microscope analysis of YMR212-GFP fusion proteins and by biochemical analysis of YMR212-GST fusion proteins).

Example 7 : CaDR325

The CaDR325 sequence is given at SEQ ID 20.

CaDR325 was cloned based on gene fragment data from the public Stanford *Candida albicans* sequencing database.

(a) 3 fragments that showed homology to *Saccharomyces cerevisiae* YDR325 were identified, the sequences of which are disclosed in SEQ ID 22, 23 and 24.

Based on these data, the following oligos were designed that allowed the verification of the database sequences and the amplification of an approx. 2200 bp internal CaDR325 fragment from genomic DNA:

cgagcatctacttgttcaaccac: hybCaYDR325ba Oligo
gaatctctggctcgctc: 325-juls Oligo
gaccgagatacacgagaat: 325-julr Oligo
ggttaaatgatcgtgatgaat: Ca325r Oligo
caacctcactgacaaatactt: Ca325s Oligo

The finally subcloned 2200 bp internal fragment was amplified by the combination hybCaYDR325ba + 325-julr oligos.

(c) 3´- and 5´- Extension of the internal fragment:

The Sanglard genomic Candida DNA library (received from RMV) in the YEP24 vector backbone was used for the amplification of 3´- and 5´- coding and non-coding sequences. This was done by using the following vector-specific oligos (directional towards the insert) and CaDR325 2200 bp fragment-specific oligos (directional towards the vector flanking sequences):

cggaattcctatcgactacgcgatcatgg : YEP24for (vector specific)

gcgaattccgatataggcgccagcaac : YEP24ba (vector specific)

acgcttccaatgtattattctcg : Oligo 1-10-A back

Claims:

1. A polynucleotide having the sequence as depicted in the sequence selected from the group consisting of SEQ ID No.2, SEQ ID No.~~4~~5, SEQ ID No.~~6~~8, SEQ ID No.~~7~~10, SEQ ID No.~~9~~8, SEQ ID No.~~10~~15, SEQ ID No.~~11~~17 or SEQ ID No.~~13~~20, homologs thereof and functional fragments thereof.

2.-The polynucleotide of claim 1 which is the gene CaNL256, homologs thereof and functional fragments thereof.

3.-The polynucleotide of claim 1 which is the gene CaBR102, homologs thereof and functional fragments thereof.

4.-The polynucleotide of claim 1 which is the gene CaIR012, homologs thereof and functional fragments thereof.

5.-The polynucleotide of claim 1 which is the gene CaMR212, homologs thereof and functional fragments thereof.

6.-The polynucleotide of claim 1 which is the gene CaDR325, homologs thereof and functional fragments thereof.

7.-The polynucleotide of claim 1 which is the gene CaOR110, homologs thereof and functional fragments thereof.

8.-The polynucleotide of claim 1 which is the gene CaJL039, homologs thereof and functional fragments thereof.

9 -A protein encoded by the polynucleotide according to claim 2 or a functional polypeptide fragment thereof.

10 -A protein encoded by the polynucleotide according to claim 3 or a functional polypeptide fragment thereof.

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9| PRTS

ESSENTIAL GENES FROM C. ALBICANS AND A METHOD FOR SCREENING ANTIMYCOTIC SUBSTANCES USING SAID GENES

The present invention relates to a method for screening for antimycotic substances in which essential genes from mycetes, particularly from Candida albicans (C.albicans) as well as functionally similar genes from other pathogenic mycetes, or the corresponding encoded proteins, are used as targets. The invention also relates to specific C. albicans genes.

The spectrum of known fungal infections stretches from fungal attack of skin or nails to potentially hazardous mycotic infections of the inner organs; Such infections and resulting diseases are known as mycosis.

Antimycotic substances (fungistatic or fungicidal) are used for treatment of mycosis. However, up to now, relatively few substances with pharmacological effects are known, such as Amphotericin B, Nystatin, Pimaricin, Griseofulvin, Clotrimazole, 5-fluoro-cytosine and Batraphene. The drug treatment of fungal infections is extremely difficult, in particular because both the host cells and the mycetes, are eucaryotic cells. Administration of drugs based on known antimycotic substances results therefore often in undesired side-effects, for example Amphotericin B has a nephrotoxic effect. Therefore, there is a strong need for pharmacologically efficient substances usable for the preparation of drugs, which are suitable for prophylactic treatments of immunodepressive states or for the treatment of an existing fungal infection. Furthermore, the substances should exhibit a specific spectrum of action in order to selectively inhibit the growth and proliferation of mycetes without affecting the treated host organism.

The aim of the present invention is to provide a method for the identification of antimycotic substances and especially for the identification of anti-Candida substances. An essential feature of this method is that essential genes from mycetes are used as targets for the screening.

The present invention thus concerns a method for screening antimycotic substances wherein an essential gene from mycetes or a functionally similar gene in another pathogenic mycete, or the corresponding encoded protein, is used as target and wherein the essential gene is selected from the group consisting of CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 and CaJL039.

According to one embodiment of the method of the invention mycete cells which express the essential gene, or a functionally similar mycete gene, to a different level are incubated with the substance to be tested and the growth inhibiting effect of the substance is determined.

According to another embodiment, said target gene or the corresponding target gene encoded protein is contacted in vitro with the substance to be tested and the effect of the substance on the target is determined.

According to another embodiment, the screened substances inhibit partially or totally the functional expression of the essential genes or the functional activity of the encoded proteins.

According to one embodiment the screened substances partially or totally inhibit the activity of dihydropneopterin aldolase (DHNA) and/or dihydropteroate synthase (DHPS) and/or 7,8-dihydro-6-hydroxymethylpterin-pyrophosphokinase (HPPK).

According to another embodiment, the mycete species are selected from the group comprising Basidiomycetes, Ascomycetes and Hyphomycetes.

According to another embodiment of the method of the invention said functional similar genes are essential genes from Candida Spp., preferably Candida albicans, or from Aspergillus Spp., preferably from Aspergillus fumigatus.

According to another aspect, the present invention concerns a polynucleotide having the sequence as depicted in SEQ ID No.2, SEQ ID No.4, SEQ ID No.6, SEQ ID No.7, SEQ ID No.9, SEQ ID No.10, SEQ ID No.11 or SEQ ID No.13, preferably SEQ ID No.2, SEQ ID No.4, SEQ ID No.6, SEQ ID No.9, SEQ ID No.10 or SEQ ID No.11, homologs thereof and functional fragments thereof.

According to another aspect, the present invention concerns a gene which is CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, preferably CaOR110, CaMR212, CaNL256, CaBR102 or CaIR012, or a functionally similar gene or a functional fragment thereof.

According to this embodiment, the functionally similar gene or homologous polynucleotide has a sequence identity, at the nucleotide level, with CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, respectively, of at least 50%, preferably of at least 60%, and most preferably of at least 70%. A functional fragment is a polynucleotide fragment that will retain the functionality of the starting product (nucleotide or gene). One example is the CaOR110 splice variant (which is also homologous to the original gene, with about 90% identity).

According to another embodiment, the functionally similar gene has a sequence identity, at the amino-acid level, with CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, respectively, encoded protein(s) of at least 40%, preferably of at least 50%, more preferably of at least 60% and most preferably of at least 70%.

These figures given for the gene apply mutatis mutandis to the polynucleotide, as far as homology and similarity.

According to another aspect, the present invention covers the protein(s) encoded by CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, respectively, gene(s) or by a functionally similar gene, or a functional polypeptidic fragment thereof.

According to another aspect, the present invention provides a plasmid containing CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, respectively, gene(s), a functionally similar gene or a functional fragment thereof

According to another aspect, the present invention provides a plasmid (bacteria containing same) deposited at the CNCM (Institut Pasteur, Paris) on 98/08/13, with the accession numbers I-2065, I-2063 and I-2064, corresponding to the CaNL256, CaBR102 and CaIR012 genes, respectively.

According to another aspect, the present invention provides a plasmid (bacteria containing same) deposited at the DSMZ (Deutsche Sammlung von Mikroorganismen und Zellkulturen, Germany) on 99/08/06 with the accession numbers DSM 12977, DSM 12976, DSM 12978 and DSM 12979, corresponding to the CaDR325, CaOR110, CaOR110 splice variant and CaMR212, respectively.

According to another aspect, the present invention provides a kit for diagnosis of fungal infections comprising a gene selected from the group consisting of CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 and CaJL039, a functionally similar gene thereof, a functional fragment thereof, the corresponding encoded protein or a functional polypeptide fragment thereof.

According to another aspect, the present invention provides an antibody directed against the protein encoded

by the CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, respectively, gene(s) or by a functionally similar gene, or a polypeptide fragment thereof.

According to another aspect, the present invention provides a polynucleotide obtainable by the process comprising the following steps:

(i) selecting an essential gene from Saccharomyces cerevisiae;

(ii) comparing the sequence of said gene with Candida Albicans genome sequences;

(iii) deducing homologuous oligonucleotides regions;

(iv) PCR amplifying the thus-obtained oligonucleotides;

(v) using the amplimers of step (iv) for detecting the complete gene of interest:

the amplimers of step (iv) are used as a probe for detecting the complete gene of interest from a Candida albicans genomic or cDNA library; or

the complete gene is obtained by 3' and 5' extension of the amplimer, e.g. by using a PCR method.

According to the invention, the first step is to identify said essential genes and starting from these thus identified genes, essential genes from other pathogenic mycetes can be identified. For practical purposes, essential genes from S. cerevisiae are first identified and starting from them, essential genes from other pathogenic fungus, especially from Candida, are obtained.

The present invention thus discloses the identification of essential genes from C.albicans and their use in a method for the screening of antimycotic substances, especially anti-Candida substances.

In order to identify essential genes of S.cerevisiae, individual genomic genes are eliminated through homologous

recombination. If the DNA segment thus eliminated concerns an essential gene, then the deletion is lethal for the S.cerevisiae cells in haploid form.

A method, wherein the studied S. cerevisiae gene is replaced by a marker gene can be used to generate the corresponding genomic deletion of S.cerevisiae and to determine the S.cerevisiae cells containing the deletion.

As a selection marker a dominant selection marker (e.g. kanamycin resistance gene) or an auxotrophic marker can for example be used. As an auxotrophic marker, it is possible to use genes coding for key enzymes of amino acid or nucleic base synthesis. For example, one can use as a selection marker the following genes from S.cerevisiae : gene encoding for the metabolic pathway of leucine (e.g.LEU2-gene), histidine (e.g. HIS3-gene) or tryptophan (e.g. TRP-1 gene) or for the nucleic base metabolism of uracil (e.g. URA3-gene).

Auxotrophic S.cerevisiae strains can be used. These auxotrophic strains can only grow on nutritive media containing the corresponding amino acids or nucleotide bases. All laboratory S.cerevisiae strains, containing auxotrophic markers can for instance be used. When diploid S.cerevisiae strains are used, then the corresponding marker gene must be homozygously mutated. Strain CEN.PK2 or isogenic derivates thereof can be used.

Strains containing no suitable auxotrophic marker can also be used such as prototrophic S.cerevisiae strains. Then a dominant selection marker e.g. resistance gene, such as kanamycin resistance gene can be used. A loxP-KanMX-loxP cassette can advantageously be used for this purpose.

For the homologous recombination replacing the whole DNA sequence or part thereof of a S.cerevisiae gene, DNA fragments are used wherein the marker gene is flanked at

the 5'- and 3'-ends by sequences which are homologous to the 5'- and 3'-ends of the studied S.cerevisiae gene.

Different processes can be used for the preparation of the corresponding DNA fragments which are also appropriate for the deletion of any specific S.cerevisiae gene. A linear DNA-fragment is used for the transformation of the suitable S.cerevisiae strain. This fragment is integrated into the S.cerevisiae genome by homologous recombination. These processes include:

1. "Conventional method" for the preparation of deletion cassettes (Rothstein, R.J. (1983) Methods in Enzymology, Vol. 101, 202-211).

2. "Conventional Method" using the PCR technique ("modified conventional method").

3. SFH (short flanking homology)- PCR method (Wach, A. et al. (1994) Yeast 10: 1793-1808; Gültner, U. et al. (1996) Nucleic Acids Research 24:2519-2524).

1. In the "conventional method" for the preparation of deletion cassettes in the S.cerevisiae genome, the gene to be studied is either already present in an appropriate vector or is integrated in such a vector. With this method, any pBR- pUC- and pBluescript®-derivates can be used for example. A major part of the target gene sequence is eliminated from the vector, for instance using appropiate restriction sites, conserving however the 3'- and 5'-regions of the studied gene inside the vector. The selected marker gene is integrated between the remaining regions.

2. In the modified form of this "conventional method", PCR is used. This method allows amplification of the 3'- and 5'-terminal regions of the coding sequence of the studied S.cerevisiae gene. This method amplifies selectively both terminal regions of the studied gene, therefore, two PCR-reactions must be carried out for each studied gene, amplifying once the 5'-end, and once the 3'-

end of the gene. The length of the amplified terminal DNA-fragment depends on the existing restriction sites. The amplified terminal ends of the studied gene have generally a length of 50 to 5000 base pairs (bp), preferably a length between 500 and 1000 bp.

As template for the PCR-reactions, genomic DNA of S.cerevisiae or wild-type genes can be used. The primer-pairs (a sense and an antisense primer, respectively) are constructed so that they correspond to the 3'-end and the 5'-end sequence of the studied S.cerevisiae gene. Especially, the primer is selected such as to allow its integration by way of appropriate restriction sites.

As vectors, pBR- pUC- and pBluescript®-derivates can be used. In particular vectors already containing a gene encoding the selection marker, are appropriate. In particular, vectors can be used, which contain genes of the selection marker HIS3, LEU2, TRP1 or URA3.

The DNA segments of the studied S.cerevisiae gene, obtained by PCR, are integrated in the vector at both sides of the selection marker, so that subsequently, as in the "conventional method", the selection marker is flanked on both ends by DNA sequences which are homologous to the studied gene.

3. Homologous recombination in S.cerevisiae takes place in a very efficient and precise manner and the length of the DNA sequence homologous to the studied S.cerevisiae gene flanking the selection marker gene can in fact be considerably shorter than with the "modified conventional method". The flanking ends homologous to the studied S.cerevisiae gene need to present a length of only about 20-60 bp, preferably 30-45 bp. The SFH-PCR method is particularly advantageous as the laborious cloning step can be obviated.

A PCR reaction is carried out on a DNA-template containing the gene for the selection marker to be used, wherein the primers are constructed so that the DNA sequence of the sense primer is homologous to the 5'-end of the selection marker sequence and so that the primer presents in addition at its 5'-end a region of preferably 40 nucleotides, which corresponds to the 5'-terminal sequence of the studied S.cerevisiae gene. The antisense primer is constructed in an analogous manner, i.e. it is complementary to the 3'-end of the gene sequence of the selection marker, wherein this primer contains at its 5'-end a region of also preferably 40 nucleotides, which corresponds to the complementary strand of the 3'-terminal coding sequence of the studied gene.

For the amplification of S.cerevisiae genes to be studied by the SFH-PCR method, vectors containing the gene for the auxotrophic marker or selection marker can be used. Especially, plasmid pUG6 is used as the template. This plasmid contains a loxP-KanMX-loxP cassette (Gültner, U. et al. (1996) Nucleic Acids Research 24: 2519-2524). In other terms, the Kanamycin resistance gene is flanked at both ends by a loxP sequence (loxP-KanMX-loxP cassette). This cassette is advantageous in that the Kanamycin resistance gene can be eventually eliminated from the S.cerevisiae genome after integration of the loxP-KanMX-loxP cassette into the S.cerevisiae gene to be studied. Cre-recombinase of bacteriophage P1 can be used for this purpose. Cre-recombinase recognizes the loxP sequences and induces elimination of the DNA located between the two loxP sequences by a homologous recombination process. As a result only one loxP sequence remains and the so-called marker regeneration occurs, i.e. the S.cerevisiae strain may be transformed again using the loxP-KanMX-loxP cassette. This is particularly advantageous, when at least

two functionally similar genes are to be deleted in order to obtain a lethal phenotype.

With the PCR-method, the PCR reaction primers are at the 3'-end a preferably 20 nucleotide long sequence, which is homologous to the sequence situated left and/or right of the loxP-KanMX-loxP cassette, and at the 5'-end a preferably 40 nucleotide long sequence, which is homologous to the terminal ends of the gene to be studied.

Using the three methods, one obtains linear deletion cassettes containing the gene encoding the selection marker, which is flanked on both sides by homologous sequences of the gene to be studied. The deletion cassettes are used for the transformation of diploid S.cerevisiae strains. The diploid strain S.cerevisiae CEN.PK2 (Scientific Research & Development GmbH, Oberursel) can be used for example for this purpose.

[CEN.PK2 Mata/MAT α ura3-52/ura3-52 leu2-3, 112/leu2-3, 112his3Δ1/his3Δ1 trp1-289/trp1-289 MAL2-8^{C}/MAL2-8^{C} SUC2/SUC2]

The strain CEN.PK2 is prepared and cultivated using known methods (Gietz, R.D. et al. (1992) Nucleic Acids Research 8: 1425; Güldener, U. et al. (1996) Nucleic Acids Research 24:2519-2524).

The cells of the S.cerevisiae strain used are transformed according to known processes with an appropriate DNA quantity of the linear deletion cassette (e.g. Sambrook et al. 1989). Thereafter, the medium in which the cells are cultivated is replaced by a new medium, a so-called selective medium, which does not contain the corresponding amino acid (e. g. histidine, leucine or tryptophan) or nucleic base (e. g. uracil) or, when using a deletion cassette containing the kanamycin resistance gene, by a medium containing geneticin (G418®) (e.g. a complete medium (YEPD) containing geneticin). Alternatively, the

transformed cells may be plated on agar plates prepared using the corresponding media. Thereby, one selects the transformed cells, in which a homologous recombination occured, since only those cells can grow under these modified conditions.

However, in most cases, only one of the two copies of the gene in the double chromosome set of a diploid S.cerevisiae strain is replaced by the DNA of the deletion cassette during the transformation, resulting in a heterozygote-diploid S.cerevisiae mutant strain, wherein one copy of the gene studied is replaced by a selection marker, while the other copy of the gene is maintained in the genome. This presents the advantage that in case of a deletion of an essential gene, due to the existence of the second copy of the essential gene, the mutant S.cerevisiae strain is still viable.

The proper integration of the deletion cassette DNA at the predetermined chromosomal gene locus (gene locus of the gene to be studied) may be checked by Southern-Blot Analysis (Southern, E.M. (1975) J. Mol. Biol. 98:503-517) or by diagnostic PCR analysis using specific primers (Güldener, U. et al. (1996) Nucleic Acids Research 24:2519-2524)

The genetic separation of individual diploid cells may be monitored by tetrad analysis. To this end, reduction division (meiosis) is induced in the diploid cells, especially heterozygote mutant strains, using known methods such as nitrogen impoverishment on potassium acetate plates (Sherman, F. et al. (1986) Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N. Y.; Guthrie, C. and Fink, G.R. (1991) Methods in Enzymology, Vol.194. Academic Press, San Diego, 3-21; Ausubel, F. M. et al. (1987) Current Protocol in Molecular Biology John Wiley and Sons, Inc., Chapter 13). Meiosis results only in asci with four

ascospores (segregated), which can be indivualized after partial enzymatic digestion of the ascospore wall with żymolyase (Ausubel et al. (1987)) by way of micromanipulators (e.g. SINGER). For example when a tetrad analysis is carried out on a heterozygote-diploid mutant strain in which an essential gene present in the double chromosome set is replaced on one chromosome by homologous recombination, then only two segregated ascospores are viable, namely those which carry the essential gene. The two remaining segregated ascospores are not viable because they lack the essential gene.

In order to check if the genes studied by this method are really essential or if the homologous recombination leads to an alteration of an essential gene adjacent to the gene locus of the gene studied, the heterozygote diploid S.cerevisiae mutant strain is transformed with a centromere plasmid containing said studied gene.

A tetrad analysis is carried out on the transformants. When four instead of two viable segregates are obtained, then the studied gene contained in the centromere plasmid can complement the defect of the two non-viable haploid S.cerevisiae cells/mutant strains, which demonstrates that the studied S.cerevisiae gene is essential.

Preferably, plasmids present in low copy number, e.g. one or two copies per cell are used as centromere plasmids. For example plasmids pRS313, pRS314, pRS315 and pRS316 (Sijkorski, R. S. and Hieter, P. (1989) Genetics 122: 19-27) or similar plasmids can be used for this purpose. Preferably, the studied genes are integrated in said plasmids including their 3'- and 5'-end non-coding regions.

Individual S.cerevisiae genes may be studied using the above-described method, their sequences being totally or partially known. The complete genomic sequence of

S.cerevisiae was made accessible to the public via the WWW (World Wide Web) on April 24, 1996.

Different possibilities exist to have access to the S.cerevisiae genomic DNA sequence via the WWW.

MIPS (Munich information Centre of Protein Sequence) Address http://speedy.mips.biochem.mpg.de/mips /yeast/

SGD (Saccharomyces Genome Database, Stanford)

Address http://genome-www.stanford.edu/Saccharomyces

YPD(Yeast Protein Database, Cold Spring Harbor)

Address http://www.proteome.com/YPDhome.html

The complete S.cerevisiae DNA sequence is also accessible via FTP (file transfer protocol) in Europe (e.g. at the address: ftp.mips.embnet.org) in the U.S.A. (address: genome-ftp.stanford.edu) or in Japan (address: ftp.nig.ac.jp).

7 essential genomic S.cerevisiae genes have been identified by this way: YDR325w, YJL039c, YOR110w, YNL256w, YBR102c, YIR012w and YMR212c

The essential genes of S.cerevisiae are then used to identify corresponding functionally similar genes in other mycetes.

By functionally similar genes in other mycete species, is meant genes which have a function similar or identical to that of the identified essential genes of S.cerevisiae. Functionally similar genes in other mycetes may, but need not be homologous in sequence to the corresponding essential S.cerevisiae genes. Functionally similar genes in other mycetes may exhibit only moderate sequence homology at the nucleotide level to the corresponding essential S.cerevisiae genes. By moderate sequence homology it is meant in the present invention genes having a sequence identity, at the nucleotide level, of at least 50%, more preferably of at least 60% and most preferably of at least 70%.

In addition, functionally similar genes in other mycetes may, but need not encode proteins homologous in sequence to the proteins encoded by the essential S.cerevisiae genes. Functionally similar proteins in other mycetes may exhibit moderate protein sequence homology to the proteins encoded by the essential S.cerevisiae genes.

By moderate protein sequence homology is meant in the present invention proteins having a sequence identity, at the amino-acid level, of a least 40%, preferably of at least 50%, more preferably of at least 60% and most preferably of at least 70%.

Genes homologous in sequence may be isolated according to known methods, for example via homologous screening (Sambrook, J. et al. (1989) Molecular Cloning Cold Spring Harbor Laboratory Press, N.Y.) or via the PCR technique using specific primers from genomic libraries and/or cDNA libraries of the corresponding mycetes.

According to one embodiment, genes homologous in sequences are isolated from cDNA libraries. In order to find out functionally similar genes in other mycetes, mRNA is isolated from mycete species to be studied according to known methods (Sambrock et al. 1989) and cDNA is synthesized according to known methods (Sambrock et al. 1989; or cDNA synthesis kits, e.g. from STRATAGENE).

The prepared cDNA is directionally integrated in a suitable expression vector.

For example, synthesis of the first cDNA strand may be carried out in the presence of primers having appropriate restriction sites in order to allow a subsequent cloning in the proper orientation with respect to the expression vector promoter. As restriction sites, any known restriction site may be used. As a primer, for instance the following primer, 50 nucleotides long may be used:

5'-GAGAGAGAGAGAGAGAGAGAACTAGTXXXXXXTTTTTTTTTTTTTTTTT-3'

The sequence $(X)_6$ represents an appropriate restriction site, for example for XhoI.

After two-strand synthesis, the cohesive ends of the double stranded cDNA are filled (blunt end) and the cDNA ends are then ligated using a suitable DNA adaptor sequence. The DNA adaptor sequence should contain a restriction site which should be different from the restriction site used in the primer for the synthesis of the first cDNA strand. The DNA adaptor may comprise for example complementary 9- or 13-mer oligonucleotides, whose ends represent the cohesive end of a restriction site. These ends may be for example a EcoRI-site:

5' XXXXXGGCACGAG 3'

3' XCCGTGCTC 5'

The single-stranded X in the adaptor sequence represent the cohesive end of a restriction site.

The cDNA provided with corresponding adaptor sequences is then cleaved using restriction endonuclease, whose recognition site was used in the primer for the synthesis of the first cDNA strand, for example XhoI. The cDNA thus obtained would have according to this example 3'-XhoI and 5'-EcoRI protruding ends and could be therefore directionally integrated into an expression vector cleaved with XhoI and EcoRI.

As expression vectors, among others, E. coli/S.cerevisiae shuttle vectors, i.e. vectors usable in E. coli as well as in S.cerevisiae are suitable. Such vectors may then be amplified for instance in E. coli. As expression vectors, those which are present in a high copy number as well as those present in a low copy number in S.cerevisiae cells can be used. For this purpose, for example vectors selected in the group consisting of pRS423

- pRS426 (pRS423, pRS424, pRS425, pRS426) and/or pRS313-pRS316 (pRS313, pRS314, pRS315, pRS316) (Sikorki, R.S. and Hieter, P. (1989) Genetics 122: 19-27; Christianson T. W. et al. (1992) Gene 110: 119-122) are suitable.

Expression vectors should contain appropriate S.cerevisiae promoters and terminators. In case they do not have these elements, the corresponding promoters and terminators are inserted in such a way that a subsequent incorporation of the generated cDNA remains possible. Particularly suitable are the promoters of S.cerevisiae genes MET25, PGK1, TPI1, TDH3, ADHI, URA3. One may use promoters of the wild-type gene in non modified form as well as promoters which were modified in such a way that certain activator sequences and/or repressor sequences were eliminated. As terminators, for example the terminators of the S.cerevisiae genes MET25, PGK1, TPI1, TDH3, ADHI, URA3 are suitable.

According to another embodiment, genes homologous in sequence are isolated from genomic libraries. Genomic DNA libraries from mycetes can be prepared according to procedures known (for example as described in Current Protocols in Molecular Biology, John Wiley and Sons, Inc). For example, genomic DNA from mycetes can be prepared using known methods for yeast cell lysis and isolation of genomic DNA (for example commercially available kits from Bio101, Inc). The genomic DNA can be partially digested using a restriction enzyme such as Sau3AI and the fragments are size-selected by agarose gel electrophoresis. DNA fragments having for example a size of 5-10kb are then purified by classical methods (as for example, using Gene Clean kit from Bio101) and inserted in a E.coli/yeast shuttle vector such as YEP24 (described e.g. by Sanglard D., Kuchler K., Ischer F., Pagani J-L., Monod M. and Bille J., Antimicrobial Agents and Chemotherapy, (1995) Vol.39 No11,

P2378-2386) cut by a restriction enzyme giving compatible ends (for example BamHI for Sau3AI-cut genomic DNA). The resulting expression library can be amplified in E.coli. However any known method, appropriate for the preparation of a genomic library, can be used in the present invention.

In order to find the genes in the studied mycete species, which are functionally similar to essential genes of S.cerevisiae, one S.cerevisiae essential gene is placed under control of a regulated promoter, either as an integrative (1) or extrachromosomal (2) gene.

1. For the integration of a regulated promoter in the S.cerevisiae genome, one replaces the native promoter of the selected essential gene by the regulated promoter, for example by homologous recombination via PCR (Güldener et al. (1996). The homologous recombination via PCR can be carried out for example in the diploid S.cerevisiae strain CEN.PK2. The successfull integration into one chromosome can be checked in haploid cells following tetrad analysis.

Using the tetrad analysis, one obtains four viable ascospores, wherein in two haploid segregates, the selected essential gene is placed under the control of the native promoter, while the essential gene in the two remaining segregates is placed under the control of the regulated promoter.

The last mentioned haploid segregates are used for the transformation with the cDNA or the genomic DNA present in the recombinant vector.

2. Using the extrachromosomal variant, the selected essential S.cerevisiae gene is first inserted in a suitable expression vector, for example a E.coli/ S.cerevisiae shuttle vector. For this purpose, the essential gene may be amplified via PCR from genomic S.cerevisiae DNA starting from the ATG initiation codon up to and including the termination codon. The primers used for this purpose may be

constructed in such a way that they contain recognition sites for appropriate restriction enzymes, facilitating a subsequent insertion under control of a regulated promoter in an expression vector.

The recombinant expression vector with the plasmid copy of the essential S.cerevisiae gene under the control of a regulated promoter is subsequently used for the transcomplementation of the corresponding mutant allele. The corresponding mutant allele may be selected from the heterozygote-diploid mutant strains prepared by eliminating, partially or totally, by homologous recombination an essential mycete gene listed above and as described above.

The expression vector with the selected essential S.cerevisiae gene is transformed in the corresponding heterozygote-diploid mutant strain carrying instead of the selected essential S.cerevisiae gene, a selection marker gene. The transformants are isolated by selection based on the auxotrophic marker contained in the expression vector used. The thus transformed heterozygote-diploid mutant strains are submitted to a tetrad analysis. One obtains four viable segregates. By retracing the corresponding markers of the mutant allele and the expression vector, the transformed wild-type segregates may be distinguished from segregates which do not contain the genomic copy of the essential gene. Segregates, which do not contain the genomic copy of the selected essential gene, are designated as trans-complemented haploid mutant strains. They are subsequently used for transformation with cDNA or genomic DNA libraries from other mycete species present in appropriate vectors.

As regulated promoters, inducible or repressible promoters may be used. These promoters can consist of naturally and/or artificially disposed promoter sequences.

As regulated promoters, for example the promoters of GAL1 gene and the corresponding promoter derivatives, such as for example promoters, whose different UAS (upstream activation sequence) elements have been eliminated (GALS, GALL; Mumberg, J. et al. (1994) Nucleic Acids Research 22:5767-5768) may be used. As regulated promoters, promoters of gluconeogenic genes may also be used, such as e.g. FBP1, PCK1, ICL1 or parts therefrom, such as e.g. their activation sequence (UAS1 and/or UAS2) or repression sequence (URS, upstream repression sequence) (Niederacher et al. (1992), Curr. Genet. 22: 636-670; Proft et al. (1995) Mol. Gen. Gent. 246: 367-373; Schüller et al. (1992) EMBO J; 11: 107-114; Guarente et al. (1984) Cell 36: 503-511).

A S.cerevisiae mutant strain modified in this manner can be cultivated under growth conditions, in which the regulated promoter is active, so that the essential S.cerevisiae gene is expressed. The S.cerevisiae cells are then transformed with a representative quantity of the library containing the studied mycete species cDNA or genomic DNA. Transformants express additionally the protein whose coding sequence is present in the recombinant vector.

The method contemplates that the growth conditions may be modified in such a way as to inhibit the regulated promoter, under the control of which is the selected essential gene. Especially, growth conditions may be changed by replacing the growth medium. When for example the GAL1 promoter or a derivate thereof is used, one can replace the galactose-containing medium (induced state) by a glucose-containing medium (repressed state).

These modified conditions are lethal for the S.cerevisiae cells in which the recombinant vector does not carry the functionally similar genomic DNA or cDNA of the studied mycete species. On the contrary, the S.cerevisiae

cells in which the recombinant vector expresses a functionally similar coding sequence of the studied mycete species, are viable, since in these cells the lethal metabolic defect is complemented by the protein encoded by the functionally similar gene.

The method contemplates that the recombinant vector (the plasmid) is isolated from the surviving transformants using known method (Strathern, J.N. and Higgins, D.R. (1991). Plasmids are recovered from yeast into Escherichia coli shuttle vectors in:Guthrie, C. and Fink, G.R. Methods in Enzymology, Volume 194. Guide to yeast genetic and molecular Biology. Academic Press, San Diego, 319-329) and the cDNA or genomic DNA is analyzed using DNA-analysis methods such as DNA sequencing. (Sanger et al. (1977), Proc. Natl. Acad. Sci. USA 74: 5463-5467)

Essential S.cerevisiae genes may thus be used for the identification of functionally similar genes and/or genes homologous in sequence in other mycetes, especially essential genes functionally similar and/or homologous in sequence in mycetes pathogenic to human, animal and plants. For this purpose for example mycetes of the classes phycomycetes or eumycetes may be used, in particular the subclasses basidiomycetes, ascomycetes, especially mehiascomycetales (yeast) and plectascales (mould fungus) and gymnascales (skin and hair fungus) or of the class of hyphomycetes, in particular the subclasses conidiosporales (skin fungus) and thallosporales (budding or gemmiparous fungus), among which particularly the species mucor, rhizopus, coccidioides, paracoccidioides (blastomyces brasiliensis), endomyces (blastomyces), aspergillus, penicilium (scopulariopsis), trichophyton (ctenomyces), epidermophton, microsporon, piedraia, hormodendron, phialophora, sporotrichon, cryptococcus, candida, geotrichum and trichosporon.

Of particular interest is the use of Candida Spp. especially Candida albicans, Candida glabrata, Aspergillus Spp., especially Aspergillus fumigatus, Coccidioides immitis, Cryptococcus neoformans, Histoplasma capsulatum, Blastomyces dermatitidis, Paracoccidioides brasiliens and Sporothrix schenckii.

Starting from the genes of S.cerevisiae, identified according to the above-described method, Applicants cloned corresponding essential genes from C.albicans i.e. CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, by the following method.

First, oligonucleotide(s) is(are) selected in the sequence of the S.cerevisiae gene or a homologous C. albicans sequence in order to amplify the corresponding fragment of C.albicans. After cloning, the obtained fragment (exhibiting a sequence of about several hundred bp) is used as a probe for screening a C.albicans (genomic) DNA library. The screening may include the following steps: clones were spread on dishes, covered with filters where the DNA was crosslinked to the filters, filters are hybridized, the positive colonies are then detected. The selected clone(s) is (are) then sequenced.

The method contemplates that essential mycete genes are used to identify substances which may inhibit partially or totally the functional expression of these essential genes and/or the functional activity of the encoded proteins. Substances may be identified in this fashion, which inhibit mycetes growth and which can be used as antimycotics, for example in the preparation of drugs.

The present invention especially covers a method for screening such inhibiting substances, wherein an essential gene from C.albicans selected from CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, or a

functionally similar gene in another pathogenic mycete or the corresponding encoded protein is used as target.

By functionally similar genes in other pathogenic mycete species, is meant genes which have a function similar or identical to that of the identified essential genes of C.albicans. Functionally similar genes in other pathogenic mycetes may, but need not be homologous in sequence to the corresponding essential C.albicans genes. Functionally similar genes in other pathogenic mycetes may exhibit only moderate sequence homology at the nucleotide level to the corresponding essential C.albicans genes. By moderate sequence homology it is meant in the present invention genes having a sequence identity, at the nucleotide level, of at least 50%, more preferably of at least 60% and most preferably of at least 70%.

In addition, functionally similar genes in other pathogenic mycetes may, but need not encode proteins homologous in sequence to the proteins encoded by the essential C.albicans genes. Functionally similar proteins in other mycetes may exhibit moderate protein sequence homology to the proteins encoded by the essential C.albicans genes.

By moderate protein sequence homology is meant in the present invention proteins having a sequence identity, at the amino-acid level, of a least 40%, preferably of at least 50%, more preferably of at least 60% and most preferably of at least 70%.

A particular feature of this method is that essential mycete genes or the corresponding encoded proteins are used as targets for the screening of the substances. The method contemplates that essential C.albicans genes as well as functionally similar genes and/or genes homologous in sequence of other pathogenic mycetes or the corresponding encoded proteins may be used as targets.

According to one embodiment of the screening method of the invention, mycetes cells are provided, which contain the essential gene used as target, and those cells are incubated with the substance to be tested. By this way, the growth inhibitory effect of this substance with respect to the essential target gene is determined.

The mycetes cells which express the essential target gene to a different degree are used, and these cells are then incubated with the substance to be tested and the growth inhibitory effect of this substance is determined.

The method includes the use of two or more mycetes cells, or strains derived therefrom, which differ in that they express the essential target gene to a different degree.

For example, two, three, four, five, ten or more mycetes cells or the corresponding mycetes strains may be comparatively analysed with respect to the growth inhibitory effect of a substance used in a defined concentration. Through such expression degree series, antimycotic substances may be distinguished from cytotoxic or inactive substances.

A particular embodiment of the method includes the use of haploid mycetes cells/ strains for the screening, especially haploid S.cerevisiae cells/ strains.

The method contemplates the integration of the essential gene selected as a target in a suitable expression vector.

As expression vectors E.coli/S.cerevisiae shuttle vectors are for example suitable. Especially vectors differing in their copy number per cell may be used. Therefore, one may use vectors, which are present in the transformed S.cerevisiae cells in a high copy number, or one can also use those with a low copy number. One embodiment comprises the use of expression vectors which

allow the integration of the target gene in the S.cerevisiae genome.

For example the vectors pRS423, pRS424,pRS425, pRS426, pRS313, pRS314, pRS315, pRS316, pRS303, pRS304, pRS305, pRS306 (Sikorki and Hieter, 1989; Christianson et al. 1992) are appropriate as expression vectors.

The vectors of the series pRS423 - pRS426 are present in a high copy number, about 50 - 100 copies/ cell. On the contrary, the vectors of the series pRS313 - pRS316 are present in a low copy number (1 - 2 copies / cell). When expression vectors from these two series are used, then the target gene is present as an extrachromosomal copy. Using the vector of the series pRS303 - pRS306 allows the integration of the target genes into the genome. Using these three different expression vector types allows a gradual expression of the studied functionally similar essential gene.

The method includes that the growth inhibitory effect of substances with respect to mycetes cells/strains is comparatively determined using expression vectors differing for instance in the copy number of the vector/ cell.

Such cells may express the essential target gene to a different degree and may exhibit a graduated reaction with respect to the substance.

The method includes also, that a target gene expression of different strength is obtained in different mycetes cells (regulated overexpression) by insertion of the target gene in the expression vector between specific selected S.cerevisiae promoters and terminators. S.cerevisiae promoters which are constitutively expressed, but with different strength, are suitable. Examples for such promoters are native promoters of S.cerevisiae genes MET25, PGK1, TPI1, TDH3, ADH1, URA3, TRP1, as well as corresponding derivatives therefrom, for example promoter

derivatives without specific activator and/or repressor sequences.

Regulated promoters are also appropriate for the graduated over-expression of the target gene. The native promoters of the GAL1 genes and/or corresponding derivates thereof, for example promoters, in which different UAS elements have been eliminated. (GALS, GALL; Mumberg et al. (1994) Nucleic Acids Research 22: 5767-5768) as well as promoters of gluconeogenic genes, for example the promoters FBP1, PCK1, ICL1, or parts thereof, for example their activator- (UAS1 or UAS2) or repressor- (URS) sequences are used in corresponding non activable and/or non repressible test promoters (Schüller et al. (1992) EMBO J. 11: 107-114) Guarente et al. (1984) Cell 36: 503-511; Niederacher et al. (1992) Curr. Genet. 22: 363-370; Proft et al. (1995) Mol. Gen. Genet. 246: 367-373).

In the expression vector terminator for example the terminator sequence of S.cerevisiae genes MET25, PGK1, TPI1, TDH3, ADHI, URA3 may be used.

The method includes that by the use of cleverly selected expression vector types and/or the preparation of suitable expression vectors, eventually using promoters of different strength and differently regulated promoters, a series of expression vectors may be constructed, all containing the same target gene, but differing in that they express the target gene to a different extent.

The method includes the transformation of the expression vector in haploid wild-type cells of S.cerevisiae. The thus obtained S.cerevisiae cells/strains are cultivated in liquid medium and incubated in the presence of different concentrations of the tested substance and the effect of this substance on the growth behaviour of the cells/strains expressing the target gene to a different degree is comparatively analysed. The method

also includes that haploid S.cerevisiae cells/strains, transformed using the respective expression vector type without target gene, are used as a reference.

The method includes that the screening of the substances can be carried out in different media using regulated promoters, especially GAL1 promoter and its derivates (GALS and GALL), since the expression degree may be largely influenced by the choice of the respective medium. Thus, the expression degree of the GAL1 promoter decreases in the following fashion: 2 % galactose > 1 % galactose + 1 % glucose > 2 % glycerine > 2 % glucose.

The effect of the substances inhibiting the growth of wild-type cells of S.cerevisiae, may be partially or totally compensated by the overexpression of the functionally similar gene of another mycete species.

According to one embodiment, the method for screening antimycotic substances is carried out in vitro by contact of an essential or functionally similar gene or the corresponding encoded protein with the substance to be tested and determination of the effect of the substance on the target. Any in vitro test appropriate for determining the interaction of two molecules, such as a hybridization test or a functional test, can be used (e.g. enzymatic tests which are described in details in Bergmeyer H.U., Methods of Enzymatic Analysis, VCH Publishers). If the screening is carried out using the encoded protein as the target, then the corresponding essential gene is inserted by any suitable method known in the art, such as PCR amplification using a set of primers containing appropriate restriction sites, (Current Protocol in Molecular Biology, John Wiley and Sons, Inc) into an expression system, such as E. coli, Baculovirus, or yeast, and the expressed protein is then completely or partially purified by a method known in the art. Any purification method

appropriate for the purification of expressed proteins, such as affinity chromatography can be used. If the target protein function is known, a functional test can then be carried out in which the effect of the antimycotic substance on the protein function is determined. If the protein function is unknown, substances which can interact with the target protein, e.g. which bind to the encoded protein, can be tested. In such a case a test such as protection of the target protein from enzymatic digestion by appropriate enzymes can be used.

According to one specific embodiment, the method for screening antimycotic substances corresponds to an enzymatic assay wherein the activity of dihydropneopterin aldolase (DHNA) and/or dihydropteroate synthase (DHPS) and/or 7,8-dihydro-6-hydroxymethylpterin-pyrophosphokinase (HPPK) is determined; the enzymatic essay can be such as diclosed in "Bergmeyer H.U., Methods in Enzymatic analysis, VCH Publishers".

Dihydropneopterin aldolase (DHNA) catalyses the conversion of 7,8-dihydroneopterin into 6-hydroxymethyl-7,8-dihydropterin (with emission of CH_2OHCHO). Dihydropteroate synthetase (DHPS) catalyses the condensation of 6-hydroxymethyl-7,8-dihydropterin pyrophosphate to para-aminobenzoic acid to form 7,8-dihydropteroate which corresponds to the second step in the three-step pathway leading from 6-hydroxymethyl-7,8-dihydropterin to 7,8-dihydrofolate. 7,8-dihydro-6-hydroxymethylpterin-pyrophosphokinase (HPPK) catalyzes the attachment of pyrophosphate to 6-hydroxymethyl-7,8-dihydropterin to form to 6-hydroxymethyl-7,8-dihydropterin pyrophosphate which corresponds to the first step in a three-step pathway leading to 7,8-dihydrofolate. All organisms require reduced folate cofactors for the synthesis of a variety of metabolites. Most microorganisms must synthesize folate de novo because they lack the active transport system of higher vertebrate cells which allows these organisms to use dietary folates. Enzymes involved in folate biosynthesis are therefore targets for a variety

of antimicrobial agents. Consequently, these enzyme activities are essential to the microorganisms, and are absent in man.

The method also includes the identification of genes which are functionally similar and/or homologous in sequence to essential C.albicans genes from humans, animals or plants. The corresponding human, animal or plant genes may optionally be used as target genes in the method in order to test if antimycotic substances exhibit an effect on these target genes.

A particular advantage of the method is that in this way substances may be identified which efficiently inhibit mycetes growth and also the influence of these substances on corresponding functionally similar genes and/or genes homologous in sequence to essential C.albicans genes from human, animal or plants may be determined.

The method includes also the possibility to check the existence of functionally similar genes and/or human, animal or plant genes homologous in sequence to the corresponding essential mycete genes, for example by checking homology of the identified essential mycete genes or parts thereof with human, animal or plant sequence genes available in data banks. In this way, it is possible to select at an early stage from the identified essential mycete genes, depending on the aim, those for which no functionally similar gene and/or no human gene homologous in sequence exist, for example.

Thereby, the method offers a plurality of possibilities to identify selectively substances with antimycotic effects, with no harmful effect on human beings.

For example, it is possible to identify substances usable for the preparation of drugs for the treatment of mycosis or prophylaxis in immunodepression states. These

substances may be used for example for the manufacture of drugs usable for the treatment of mycotic infections, which occur during diseases like AIDS or Diabetes. Substances which may be used for the fabrication of fungicides, especially of fungicides which are harmless for humans and animals, can also be identified.

Furthermore, the method offers the possibility to identify antimycotic substances, which selectively inhibit growth of specific mycete species only.

The screening method is particularly advantageous inasmuch as it is sufficient to know whether the genes are essential, one does not need any additional information regarding the function of the essential genes or the function of the encoded proteins. In addition, it is particularly advantageous for the identification of functionally similar genes to essential S.cerevisiae gene, in other mycetes where the DNA sequence is not available for many of these genes.

According to another aspect the invention provides an antibody directed against the protein encoded by the CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039, gene or a polypeptidic fragment thereof. The term "antibody" encompasses monoclonal and polyclonal antibodies. Said antibodies can be prepared by method well known in the art such as those disclosed in "Antibodies, a laboratory manual", Ed. Harbow and David Lane. Cold Spring Harbor Laboratory Eds., 1988.

According to another aspect the present invention provides a kit for the diagnosis of fungal infections comprising a gene selected from the group consisting of CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 and CaJL039, a functionally similar gene thereof, a functional fragment thereof, the corresponding encoded protein, a functional polypeptide fragment thereof or an antiboby

directed against the protein encoded by CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 or CaJL039 gene or by a functionally similar gene, or a polypeptidic fragment thereof. Such kits can be prepared using any suitable method well known in the art.

Examples

Example 1 : CaNL256

The Internet site of Standford (http://candida.standford.edu/) gives access to preliminary sequences of the genome of C. albicans. One of these sequences has homology with the YNL256 gene of S. cerevisiae. Two oligonucleotides were selected in this sequence (5'-ATTCATCCCATCAGTGCAGAAAG-3' and 5'-ATTGACCAATAGCTCTAATTAATG-3') in order to amplify the corresponding fragment of C. albicans. After cloning, we obtained a sequence of 399 bp close to the expected sequence (SEQ ID NO:1). The deduced protein was compared with the one of YNL256, evidencing 53% similarity and 43% identity (fig.1). This fragment of 399 bp of C. albicans was used as a probe for screening a genomic library of C. albicans. The latter was prepared by partial digestion of genomic DNA of C. albicans by Sau3AI and cloning into the YEP24 vector at the BamHI site. The clones of the library were then spread at a density of 2000 clones per dish. Each dish was covered by a nitrocellulose filter which was then successively treated with: NaOH, 0.5M, 5 minutes; Tris, 1M, pH 7.7, 5 minutes; Tris, 0.5M, pH 7.7, Nacl, 1.25M, 5 minutes. After drying, the filters were kept for 2 hours at 80°C. Prehybridization and hybridization were carried out in a buffer of 40% formamide, 5xSSC, 20 mM Tris pH 7.7 1xDenhardt 0.1% SDS. The probe was labeled with 32P with the RediPrime kit and dCTP from Amersham UK. Hybridization took place over 17 hours at 42°C. The filters were then washed in 1x SSC, 0.1% SDS, three times

for 5 minutes at room temperature and then twice for 30 minutes at 60°C, and were then submitted to autoradiography overnight. The colonies corresponding to the spots obtained were reisolated by re-spreading at low density followed by further hybridization. Three clones were thus obtained (out of 40,000), which were sequenced on an ABI 377 apparatus. The sequences were compiled using the ABI software and then analysed using the GCG software package. One of these three clones turned out to contain the complete coding sequence corresponding to the probe used; this gene was called CaNL256, whose sequence is represented in SEQ ID NO:2. CaNL256 has 52% of nucleotides identical to YNL256 of S. cerevisiae. The coding region is shorter at the N-terminus. For translation to amino acids, account was taken of the fact that, in C. albicans, the CTG codon is translated to Serine (there are 3 CTG codons in CaNL256). The deduced protein had 40% amino acids identical with YNL256 of S. cerevisiae and 41% with FAS (folic acid synthase) of Pneumocystis carinii. Investigation into the databases using the Blast software showed homology of two parts of the CaNL256 protein with, respectively, the bacterial enzymes Dihydropteroate Synthase (EC 2.5.1.15) (DHPS) of Haemophilus influenzae, Staphylococcus haemolyticus, Neisseria meningitidis, Streptococcus pneumoniae, Bacillus subtilis, Clostridium acetobutylicum, Escherichia coli, Mycobacterium leprae (P value less than e-28) and 7,8-dihydro-6-hydroxymethylpterin-pyrophosphokinase (EC 2.7.6.3) (HPPK) of Bacillus subtilis, Escherichia coli, Haemophilus influenzae, Streptococcus pneumoniae (P value less than e-20). The units characteristic of DHPS and HPPK are also found in CaNL256.

Example 2 : CaBR102

The Internet site of Stanford (http://candida.stanford.edu/) give access to preliminary sequences of the genome of C. albicans. One of these sequences has homology with the YBR102 gene of S.cerevisiae. Two oligonucleotides were selected in this sequence (5'-AGTATTCAATTGGGTATTCC-3' and 5'-CCGGCATCATCAGTAACTCC-3') in order to amplified the corresponding fragment of C. albicans. After cloning, we obtained a sequence of 647 bp (SEQ ID NO:3). The deduced protein was compared with the one of YNL102, evidencing 35% similarity and 26% identity (fig.2). This fragment was amplified using Pfu polymerase (Stratagene). The PCR product was purified (High Pure PCR Product Purification Kit, Boehringer Mannheim) and used as a probe for screening a C. albicans genomic DNA library. The latter was prepared by partial digestion of C. albicans genomic DNA with SauIIIA and cloning into the YEP-24TRP1 vector at the BamHI restriction site. 40,000 clones of the library were then spread at a density of 2000 clones per dish. Each dish was covered by a nitrocellulose filter (Membrane Hybond N^+, Amersham) which was then successively treated with : 1.5 M NaCl/0.5 M NaOH, 5 minutes; 1.5 M NaCl/0.5 M Tris-HCl pH 7.2/1 mM EDTA, 3 minutes, twice; DNA was crosslinked to the filters (Amersham Life Science, ultra violet crosslinker). The probe (100 ng) was labelled with ^{32}P using the RediPrime kit and dCTP (Amersham Life Science). The filters were hybridized in a buffer containing 30% formamide, 5 x SSC, 5% Denhart's solution, 1% SDS, 100 μg /ml salmon sperm DNA and a probe concentration of 10^6 cpm/ml at 42°C for 16 h. The membranes were then washed three times at room temperature in 2 x SSC/0.1% SDS for 5 minutes each and three times in 1 x SSC/0.1% SDS at 60°C for 20 minutes each. the filters were then exposed overnight to an X-ray

film. The colonies corresponding to the positives clones were isolated and screened a second time by the same procedure. Two positives clones were finally obtained, which were sequenced on an ABI377 apparatus. the sequences were compiled using ABI software and then analysed using the GCG software package. The nucleotide sequences of these two clones were identical and contained the complete coding sequence corresponding to the probe used, this gene was called CaBR102, whose sequence is represented in SEQ ID No:4. The translation of this nucleotide sequence was examined, account was taken of the fact that in C. albicans the CTG codon is translated to serine (there are 3 CTG codons in CaBR102). The deduced protein has 24% identity to S. cerevisiae gene YBR102.

Example 3 : CaIR012

Chromosomal DNA from the C. albicans strain Caf2-1 was isolated using Yeast Cell Lysis prep Kit and Genome DNA Kit from BIO101. A 343 bp fragment from C. albicans genomic DNA (SEQ ID NO:5) was amplified with the oligonucleotide primers CaYIR012-5' (5'-GACGTCGTAGACGATACTCAAGAAG-3') and CaYIR012-3' (5'-CTGCAGTAAACCCTCCAGATATAACAG-3') by PowerScript DNA polymerase (PAN Systems GmbH) using the hot start technique. The PCR product was purified from the agarose gel and labeled with fluorescein (Gene image random prime labelling module, Amersham Life Science) according to the manufacturer´s instructions. Plasmid DNA from E.coli was isolated using Qiagen columns as recommended by the manufacturer. Screening the λZAPII C. albicans cDNA library was performed following the manufacturer's instructions (Stratagene Ltd.). Nylon filters (Schleicher&Schuell) were lifted from LB-plates (150 mm) with 15000 pfu/plate, denatured 5 min in 1.5M NaCL, 0.5M NaOH, neutralized 3 min in 1.5M NaCl, 0.5M Tris-HCl pH8.0, washed 3 min in 0.2 M Tris-HCl pH 7.5, 2xSSC and DNA was

crosslinked to the filters (Stratagene UV crosslinker). The filters were prehybridized 4 h at 60 °C and hybridized with the fluorescein-labeled DNA probe overnight at 60 °C. Detection was performed with Anti-fluorescein AP conjugate (Signal amplification module for the FluorImager, Amersham LIFE SCIENCE) and analysed after 20 h with a Fluorimager (Storm 860, Molecular Dynamics). Positive plaques were picked and incubated with 0.5 ml SM-buffer (100mM NaCl, 8 mM $MgSO_4$, 50 mM Tris-HCl pH7.5, 0,01% gelatin). The selected clones were diluted, titered with host cells XL1-Blue and screened and purified a second time by the same procedure. Finally, the pBluescript SK(-) phagemid containing the DNA insert of interest was rescued by the ExAssist Helper Phage system according to the Stratagene protocol. From a total of 75000 screened plaques, 3 positive clones were identified. pBluescript SK (-) phagemid DNA was isolated, sequenced with T3 and T7 primers and the sequences were extended with custom-synthesized oligonucleotide primers. Nucleotide sequence analyses were performed with the Gene Data software package (Gene Data AG, Basel Switzerland). Similarity searches with the Swissprot database were conducted with the BLAST program (Gish, Warren and David J. States (1993). Identification of protein coding regions by database similarity search. Nat. Genet. 3:266-72.). One of these three clones turned out to contain the complete coding sequence corresponding to the probe used; this gene was called CaIR1012, whose sequence is represented in SEQ ID NO:6.

Example 4: CaJL039

The CaJL039 sequence is depicted in SEQ ID No 7.

The CaJL039 gene was cloned based on gene fragment data issued from the public Stanford *Candida albicans* sequencing database.

(a) A fragment that showed homology to *Saccharomyces cerevisiae* YJL039c was identified, the sequence of which is given in SEQ ID No 8.

Using the procedure disclosed in example 3 with the oligonucleotide primer pair (Ca039s: TAG CTC AAC CTA CCA CCA ATC /Ca039r: ATC ACA AGA CTG TCA ATG TAA AT), a short PCR fragment (234 base pairs long) was amplified for screening a Candida albicans cDNA lambda ZAP II library (gift of Alistair Brown, Aberdeen).

Three positive clones of the 3' coding region were obtained.(# 21t7, 11t3, 21t3).

(b) 3'- and 5'- extension of the internal fragment using the primer walking method

The Sanglard genomic Candida DNA library with the YEp24 vector backbone was used for further amplification of 3'- and 5'-coding sequences. Amplification was carried out by using the following vector-specific oligonucleotide primers and CaJL039 fragment-specific primers:

cggaattcctatcgactacgcgatcatgg: YEp24for (vector specific)

gcgaattccgatataggcgccagcaac: YEp24ba (vector specific)

caattgctttgactcgggtgttattaagt: Ca039-51 (CaJL039: 5'fishing)

tcttggcacaacttgataagaatctgt: Ca039-52 (")

taggtgtacgcgaaagccaagtagaac:Ca039-53 (")

ttgttaatcgtacacctaaggtgttgac: Ca039-31 (CaJL039: 3'fishing)

ttgcagattgatgctagcaatgtatttg: Ca039-32 (")

Using the technique of primer walking, the complete 5'-sequence could be amplified (clone 14b-1-1 and clone 17b-3-4).

The missing 3'-sequence was available from GTC PathoGenome Release 5.0, contig #2830.

An interacting protein (C82, component for RNA polymerase III in yeast) has been identified.

Example 5: CaOR110

5.1. CaOR110

The CaOR110 sequence is depicted in SEQ ID No 9.

CaOR110 was cloned based on gene fragment data issued from the public Stanford *Candida albicans* sequencing database.

(a) A small ScOR110-homologous fragment was used in a hybridization experiment to identify CaOR110 clones in a *Candida Albicans* lambda ZAPII cDNA library (from Alistair Brown). Alignement of Candida Albicans CaOR110 sequence with the fragment used for hybridization is given in figure 3. The homologous fragment sequence is given in SEQ ID No. 17.

(b) 3´- and 5´- Extension of the internal fragment:

The Sanglard genomic Candida DNA library (received from RMV) in the YEP24 vector backbone was used for the amplification of 3´- and 5´- coding and non-coding sequences. This amplification was done by using the vector-specific oligos (directional towards the insert) and CaOR110 fragment-specific oligos (directional towards the vector flanking sequences) described below:

cggaattcctatcgactacgcgatcatgg : YEP24for

gcgaattccgatataggcgccagcaac : YEP24ba

cgggatccggtaaccaattggatctataaccgtg : 110-ba-150

gcggatcctggtgcccttggtggtgaatg : CaYOR110A

gcggatccctcacaatatgacgattgaaact : CaYOR110B

ggcgtcgactcaggcgccagttttacgtacttcaaattcatc : CaYOR110C

tgtgaattcttgacacagggtga : CaYOR110D

caaaccttcagcacaactcca : CaYOR110E,

The finaly assembled sequence that included also 3´- and 5´- non-coding sequences was verified by sequencing. The coding region was subcloned into the p414RSGALL-vector.

The map is depicted in Fig. 4.

The homologous yeast ORF (YOR110w) has been described as the transcription factor subunit TFC7 interacting with TFC1 in the TFIIIC polymerase complex (Manaud et al., 1998, Mol. Cell. Biol. 18; 3191-3200).

5.2. CaOR110 splice variant

For CaOR110, an additional splice variant was identified. The clones for the splice variant of CaOR110 were obtained from a Candida albicans cDNA library.

The sequence is depicted in SEQ ID No.10.

The splice variant uses the donor site "gtacgt" at position 907 of the original CaOR110 sequence. Acceptor site is at 1047. The map is disclosed in Fig. 5.

The alignement of the original CaOR110 and the splice variant is given in fig. 6.

Example 6 : CaMR212

The CaMR212 sequence is depicted in SEQ ID No. 11.

(a) CaMR212 was cloned based on gene fragment data from the public Standford *Candida albicans* sequencing database.

The sequence of a fragment showing homology (Blast search) to the *Saccharomyces cerevisiae* gene YMR212c is given in SEQ ID 12.

Based on these data, the following oligos were designed that allow amplification of this fragment (490 bp-fragment) from genomic *Candida albicans* DNA.

Oligos:

CaYMR212for: 5´- cacctgtgaacaacccaccatc-3´

CaYMR212back: 5´- gaatatcctttttaactcaagag -3´

(b) 3´- and 5´- extension of this internal fragment from CaMR212

For this purpose, genomic Candida DNA libraries from Dominique Sanglard (received from RMV) were used. The YEp24 backbone of this library was used to amplify the 3´- and 5´- coding and non coding sequences with PCR. This was done

by using oligos specific for the CaMR212 490 bp-fragment (directional towards the vector flanking regions) and vector-specific oligos (directional towards the insert).

Oligos:

YEP24for (vector specific):

5´-cggaattcctatcgactacgcgatcatgg

YEP24ba (vector specific):

5´-gcgaattccgatataggcgccagcaac

Primer YEp24for and CaMR212for gave a 500 bp fragment, encoding 5´-UTR and the 5´coding region from CaMR212.

Using primer YEp24 for and CaMR212back a 1400 bp CaMR212-fragment was amplified. Using the sequence of this 1400 bp-fragment the following new primers, specific for this fragment were designed.

Oligos:

Ca212-1: 5´- gctttcccagcaggataacattg

Ca212-2: 5´- tgagttataatgcagctgttgg

Ca212-3: 5´- catctcgtgtgaacatgattgg

Primers YEP24 for and Ca212-3 gave a 1600 bp fragment, coding for the 3´- coding region and the 3´UTS region.

With the 3 PCR fragments the 2900 bp sequence(including coding and 3´and 5´-non-coding sequences) was assembled. With the following new primers the coding sequences was amplified from genomic DNA and cloned into p413GALL-vector.

Oligos for amplifying coding region:

Ca212for: 5´- agtttcttcaacttccagatccaag

Ca212back: 5´- gtatatttgcaactgtctctctctc

The yeast homolog YMR212c plays a role in cell wall function because the knockout can be rescued in 1M sorbitol. In addition, YMR212c unger GAL-promoter regulation shows an increased sensitivity versus Congo Red and Calcofluor White. YMR212c is an integral membrane protein and localizes to the plasma membrane (demonstrated

by microscope analysis of YMR212-GFP fusion proteins and by biochemical analysis of YMR212-GST fusion proteins).

Example 7 : CaDR325

The CaDR325 sequence is given at SEQ ID 13.

CaDR325 was cloned based on gene fragment data from the public Stanford *Candida albicans* sequencing database.

(a) 3 fragments that showed homology to *Saccharomyces cerevisiae* YDR325 were identified, the sequences of which are disclosed in SEQ ID 14, 15 and 16.

Based on these data, the following oligos were designed that allowed the verification of the database sequences and the amplification of an approx. 2200 bp internal CaDR325 fragment from genomic DNA:

cgagcatctacttgttcaaccac: hybCaYDR325ba Oligo
gaatctctggctcgctc: 325-juls Oligo
gaccgagatacacgagaat: 325-julr Oligo
ggttaaatgatcgtgatgaat: Ca325r Oligo
caacctcactgacaaatactt: Ca325s Oligo

The finally subcloned 2200 bp internal fragment was amplified by the combination hybCaYDR325ba + 325-julr oligos.

(c) 3´- and 5´- Extension of the internal fragment:

The Sanglard genomic Candida DNA library (received from RMV) in the YEP24 vector backbone was used for the amplification of 3´- and 5´- coding and non-coding sequences. This was done by using the following vector-specific oligos (directional towards the insert) and CaDR325 2200 bp fragment-specific oligos (directional towards the vector flanking sequences):

cggaattcctatcgactacgcgatcatgg : YEP24for (vector specific)

gcgaattccgatataggcgccagcaac : YEP24ba (vector specific)

acgcttccaatgtattattctcg : Oligo 1-10-A back

ggatgccaatttccctga :	Oligo 1-10-B for
catccagaagatataacggct :	Oligo 1-10-C for
tgcataatctactcagcgaca :	Oligo 1-10-D back
gtggttgaacaagtagatgctcg :	Oligo 1-10-E for
gcgcttgaaaccactagtgaattg :	Ca325Klon_2_Fo
caattcactagtggtttcaagcgc :	Ca325Klon_3_Ba

The finally assembled 4700 bp sequence that included also 3´- and 5´- non-coding sequences were verified by sequencing. The coding region was subcloned into the p413RSGALL-vector.

The map is disclosed in fig. 7.

Sequences numbers are identified in field 130 of the sequence listing.

Claims:

1. A polynucleotide having the sequence as depicted in the sequence selected from the group consisting of SEQ ID No.2, SEQ ID No.4, SEQ ID No.6, SEQ ID No.7, SEQ ID No.9, SEQ ID No.10, SEQ ID No.11 or SEQ ID No.13, homologs thereof and functional fragments thereof.

2.-The polynucleotide of claim 1 which is the gene CaNL256, homologs thereof and functional fragments thereof.

3.-The polynucleotide of claim 1 which is the gene CaBR102, homologs thereof and functional fragments thereof.

4.-The polynucleotide of claim 1 which is the gene CaIR012, homologs thereof and functional fragments thereof.

5.-The polynucleotide of claim 1 which is the gene CaMR212, homologs thereof and functional fragments thereof.

6.-The polynucleotide of claim 1 which is the gene CaDR325, homologs thereof and functional fragments thereof.

7.-The polynucleotide of claim 1 which is the gene CaOR110, homologs thereof and functional fragments thereof.

8.-The polynucleotide of claim 1 which is the gene CaJL039, homologs thereof and functional fragments thereof.

9 -A protein encoded by the polynucleotide according to claim 2 or a functional polypeptide fragment thereof.

10 -A protein encoded by the polynucleotide according to claim 3 or a functional polypeptide fragment thereof.

11 -A protein encoded by the polynucleotide according to claim 4 or a functional polypeptide fragment thereof.

12 -A protein encoded by the polynucleotide according to claim 5 or a functional polypeptide fragment thereof.

13 -A protein encoded by the polynucleotide according to claim 6 or a functional polypeptide fragment thereof.

14 -A protein encoded by the polynucleotide according to claim 7 or a functional polypeptide fragment thereof.

15 -A protein encoded by the polynucleotide according to claim 8 or a functional polypeptide fragment thereof.

16.-A plasmid deposited at the CNCM with the accession number I-2065.

17.-A plasmid deposited at the CNCM with the accession number I-2063.

18.-A plasmid deposited at the DSMZ with the accession number DSM 12977.

19.-A plasmid deposited at the DSMZ with the accession number DSM 12976.

20.-A plasmid deposited at the DSMZ with the accession number DSM 12978.

21.-A plasmid deposited at the DSMZ with the accession number DSM 12979.

22.- An antiboby directed against the protein of claim 9 or a functional polypeptide fragment thereof.

23.- An antiboby directed against the protein of claim 10 or a functional polypeptide fragment thereof.

24.- An antiboby directed against the protein of claim 11 or a functional polypeptide fragment thereof.

25.- An antiboby directed against the protein of claim 12 or a functional polypeptide fragment thereof.

26.- An antiboby directed against the protein of claim 13 or a functional polypeptide fragment thereof.

27.- An antiboby directed against the protein of claim 14 or a functional polypeptide fragment thereof.

28.- An antiboby directed against the protein of claim 15 or a functional polypeptide fragment thereof.

29.-A polynucleotide obtainable by the process comprising the following steps:

(i) selecting an essential gene from Saccharomyces cerevisiae;

(ii) comparing the sequence of said gene with Candida Albicans genome sequences;

(iii) deducing homologuous oligonucleotides regions;

(iv) PCR amplifying the thus-obtained oligonucleotides;

(v) using the amplimers of step (iv) for detecting the complete gene of interest;

and homologs thereof and functional fragments thereof.

30.-The polynucleotide of claim 29, in which step (v) is comprised of the step of using the amplimers of step (iv) as a probe for detecting the complete gene of interest from a Candida albicans genomic library.

31.-The polynucleotide of claim 29, in which step (v) is comprised of the step of using the amplimers of step (iv) as a probe for detecting the complete gene of interest from a Candida albicans cDNA library.

32.-The polynucleotide of claim 29, in which step (v) is comprised of the step of 3' and 5' extension of the amplimer using a PCR method.

33.-A method for the screening of antimycotic substances wherein an essential gene from mycetes or a functionally similar gene from another pathogenic mycete, or the corresponding encoded protein, is used as target and wherein the essential gene is selected from the group consisting of CaNL256, CaBR102, CaIR012, CaMR212, CaDR325, CaOR110, CaJL039, homologs thereof and functional fragments thereof.

34.-The method of claim 33 wherein mycete cells which express the essential gene, or a functionally similar mycete gene, to a different level are incubated with the substance to be tested and the growth inhibiting effect of the substance is determined.

35.-The method of claim 33 wherein said target gene or the corresponding target encoded protein is contacted in vitro with the substance to be tested and the effect of the substance on the target is determined.

36.-The method according to claim 33 wherein the screened substances partially or totally inhibit the functional expression of the essential genes or the functional activity of the encoded proteins.

37.-The method according to claim 33 wherein the screened substances partially or totally inhibit the activity of dihydropneopterin aldolase (DHNA).

38.-The method according to claim 33 wherein the screened substances partially or totally inhibit the activity of dihydropteroate synthase (DHPS).

39.-The method according to claim 33 wherein the screened substances partially or totally inhibit the activity of 7,8-dihydro-6-hydroxymethylpterin-pyrophosphokinase (HPPK).

40.-The method according to claim 33 wherein the mycete species are selected from the group comprising Basidiomycetes, Ascomycetes and Hyphomycetes.

41.- The method according to claim 33, wherein said functionally similar genes are essential genes from Candida Spp, or Aspergillus Spp.

42.- The method according to claim 41, wherein said functionally similar genes are essential genes from Candida albicans, or Aspergillus fumigatus.

43.- A kit for diagnosis of fungal infections comprising a gene selected from the group consisting of CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 and CaJL039, a functionally similar gene thereof, a functional fragment thereof, the corresponding encoded protein or a functional polypeptidic fragment thereof, or an antiboby directed against the protein encoded by the gene selected from the group consisting of CaOR110, CaMR212, CaNL256, CaBR102, CaIR012, CaDR325 and CaJL039, or by a functionally similar gene, or a polypeptidic fragment thereof.

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(54) Title: ESSENTIAL GENES FROM C. ALBICANS AND A METHOD FOR SCREENING ANTIMYCOTIC SUBSTANCES USING SAID GENES

(57) Abstract: The present invention concerns essential genes from C. albicans and their use in a method for the screening of antimycotic substances.

Fig.1

```
                    .         .         .         .
  1 ............................IHPISAESLHSHLQQLINDKPQ  22
                                :||:.|| :  ||.|| . .
451 PDLNIPHPRMLERTFVLEPLCELISPVHLHPVTAEPIVDHLKQLYDKQHD 500
                    .         .         .         .
 23 ETV........QESSDLLQFIPVSRLPVKDNILKFDQINHKSPTLIMGIL  64
    |            |     .|:        |          ||| || |
501 EDTLWKLVPLPYRSGVEPRFLKFKTATKLDEFTGETNRITVSPTYIMAIF 550
                   . .        .         .         .
 65 NMTPDSFSDGGKHFG...KELDNIVKQA.EKLVSEGATIIDIGGVSTRPG 110
    | |||||||||.||      :|..|:|    : |     . |||:|| ||||
551 NATPDSFSDGGEHFADIESQLNDIIKLCKDALYLHESVIIDVGGCSTRPN 600
                    .         .         .         .
111 SVEPTEEEELERVIPLIRAIRQS........................... 133
    |:: .||||: | ||||:|||:|
601 SIQASEEEEIRRSIPLIKAIRESTELPQDKVILSIDTYRSNVAKEAIKVG 650
```

Fig.2

```
             .         .         .         .         .
251 NDLNEVLDQCTKIAEKRLQLQDQIDQERQGNFNNVESHSNSPALLPPLKA 300
                                                   :.
  1 .............................................KSIQL 5

             .         .         .         .         .
301 GQNGNLMRRDRSSVLILEKFWDTELDQLFKNVEGAQKFINSTKGRHILMN 350
    |   |  ::||||:::|.| ||.:|  |||.|:|| ||:     |||.
  6 GIPSN.KKKDRSSIMVLKKMWDSQLQSLFKHVDGASKFVQPLPNRHIVAE 54

             .         .         .         .         .
351 SANWMELNTTTGKPLQMVQIFILNDLVLIADK...SRDKQNDFIVSQCYP 397
    |  | |.|    ||     :|| |||:||| |   |  .:     |
 55 SGRWFEVNVGNWKPSYPTHLFIFNDLILIAVKKSSSSSQEPTTGGSNGGS 104

             .         .         .         .         .
398 LKDVTVTQEEFSTKRLLFKFSNSNSSLYECRDADECSRLLDVI..RKAKD 445
       .   |    |.  | .  .      .    .  |: |  :      |
105 KSRLQAVQCWPLTQVSLQQIKSPKKDDDKMYFINLKSKSLSYVYLTDRYD 154

             .         .         .         .         .
446 DLCDIFHVEEENSKRIRESFRYLQSTQQTPGRENNRSPNKNK..RRSMGG 493
        :     .    . :| | | |   .|   |  |  . :  | |:
155 HFVKVTEAFNKGRNEMIQSERLLDSRLSSPSNNNGDSKEEKRQLRESLRN 204

             .         .         .         .         .
494 SITPGRNVTGAMDQYLLQNLTLSMHSRPRSRDMSSTAQRLKFLDEGVEEI 543
    |      ||          .|
205 SGNYKEGVTDDAGGAATG*VT............................. 225
```

FIG.3

```
 301 ACCCATTGCTGAAATGTTGGACTTGAAGATTGCTTTAGAAAGAGGAGTTGGTGAATGGTT

   0 ------------------------------------------------------------

 361 TCGTAAAAATAGAGATACCAAACCAGTTCCCGGTGATTACACACAATTGAGAACATTTTT

   0 ------------------------------------------------------------

 421 CGATAAATTATTGATCGATGAAGATACTTGGCCAAGAGATAACTTAAATGTTATACCTAA

   0 ------------------------------------------------------------

 481 TATTGAAGGAGAAGATTATGATGAAATCTACGATCGTGCCAAATTGTTTTGGAAAAAGTT

   0 --------------------------------TTAAATATGTGTTGATAGTTACACATGC
                                     ||||| ||||||||||||||||||||||
 541 TATTCCTGAATTTGAAAAGAAATTCCCCGAAATTAAAAATGTGTTGATAGTTACACATGC

  29 AGCAACGAAAATTGCTTTAGGATCAGCTTTATTACAGTTAAAATCAGTTACTGATGTTAT
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 601 AGCAACGAAAATTGCTTTAGGATCAGCTTTATTACAGTTAAAATCAGTTACTGATGTTAT

  89 AGATGATAATCAAACTGTGTTACGTGCTGGTGCATGTTCATTATCCAAATTTGTTAGAGA
     ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 661 AGATGATAATCAAACTGTGTTACGTGCTGGTGCATGTTCATTATCCAAATTTGTTAGAGA

 149 TGGCGAAGATAAAACCAATCATACTATTCAATGGAAAATTGTCATGAATGGTAATTGTGA
     ||||||||||||||||||| ||||||||||||||||||||||||||||||||||||||||
 721 TGGCGAAGATAAAACCAATGATACTATTCAATGGAAAATTGTCATGAATGGTAATTGTGA

 209 ATTCTTGACACAGGGTGAAGAAATGAAT--------------------------------
     |||||||||||||||||||||||||||
 781 ATTCTTGACACAGGGTGAAGAAATGAACTGGGATTTCCGTCGTGGTGTTGAAGCCGGGTC
```

FIG.4

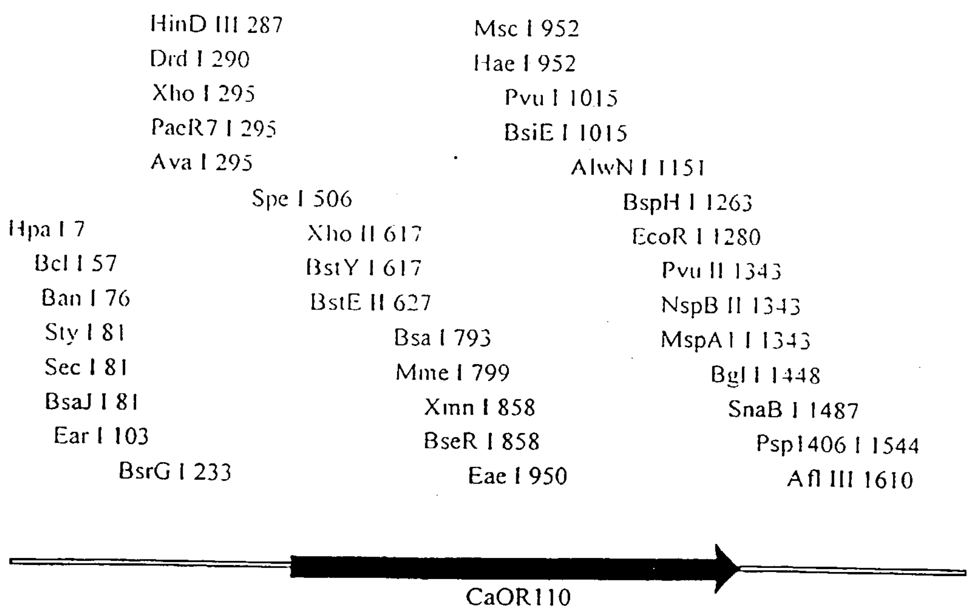
HinD III 287
Drd I 290
Xho I 295
PacR7 I 295
Ava I 295
Spe I 506
Hpa I 7
Bcl I 57
Ban I 76
Sty I 81
Sec I 81
BsaJ I 81
Ear I 103
BsrG I 233
Xho II 617
BstY I 617
BstE II 627
Bsa I 793
Mme I 799
Xmn I 858
BseR I 858
Eae I 950
Msc I 952
Hae I 952
Pvu I 1015
BsiE I 1015
AlwN I 1151
BspH I 1263
EcoR I 1280
Pvu II 1343
NspB II 1343
MspA1 I 1343
Bgl I 1448
SnaB I 1487
Psp1406 I 1544
Afl III 1610
CaOR110

FIG.5

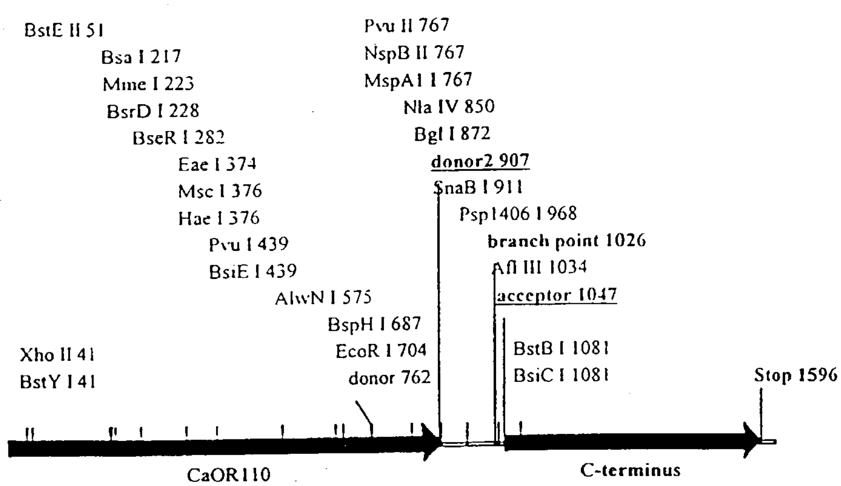
BstE II 51
Bsa I 217
Mme I 223
BsrD I 228
BseR I 282
Eae I 374
Msc I 376
Hae I 376
Pvu I 439
BsiE I 439
AlwN I 575
BspH I 687
EcoR I 704
donor 762
Xho II 41
BstY I 41
Pvu II 767
NspB II 767
MspA1 I 767
Nla IV 850
Bgl I 872
donor2 907
SnaB I 911
Psp1406 I 968
branch point 1026
Afl III 1034
acceptor 1047
BstB I 1081
BsiC I 1081
Stop 1596
CaOR110
C-terminus

FIG.6

```
  1 ATGACGATTGAAACTATTTATATCGCAAGACACGGTTATAGATCCAATTGGTTACCACCA   60
    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
  1 ATGACGATTGAAACTATTTATATCGCAAGACACGGTTATAGATCCAATTGGTTACCACCA   60

 61 CCACACCCACCAAATCCTACTGGTATTGACAGTGACCCGGCTTTAGCACCACATGGTGTT  120
    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
 61 CCACACCCACCAAATCCTACTGGTATTGACAGTGACCCGGCTTTAGCACCACATGGTGTT  120

121 GAACAAGCCCAACAGTTAGCTGCCTATCTTACATCATTACCTACACATGAAAAGCCTGAA  180
    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
121 GAACAAGCCCAACAGTTAGCTGCCTATCTTACATCATTACCTACACATGAAAAGCCTGAA  180

181 TTTATTATTGCTTCACCTTTTTATCGTTGTATAGAAACGTCGAGACCCATTGCCGAAATG  240
    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
181 TTTATTATTGCTTCACCTTTTTATCGTTGTATAGAAACGTCGAGACCCATTGCCGAAATG  240

241 TTGGACTTGAAGATTGCTTTAGAAAGAGGAGTTGGTGAATGGTTTCGTAAAAATAGAGAT  300
    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
241 TTGGACTTGAAGATTGCTTTAGAAAGAGGAGTTGGTGAATGGTTTCGTAAAAATAGAGAT  300

301 ACCAAACCAGTTCCCGGTGATTACACACAATTGAGAACATTTTTCGATAAATTATTGATC  360
    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
301 ACCAAACCAGTTCCCGGTGATTACACACAATTGAGAACATTTTTCGATAAATTATTGATC  360

361 GATGAAGATACTTGGCCAAGAGATAACTTAAATGTTATACCTAATATTGAAGGAGAAGAT  420
    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
361 GATGAAGATACTTGGCCAAGAGATAACTTAAATGTTATACCTAATATTGAAGGAGAAGAT  420

421 TATGATGAAATCTACGATCGTGCCAAATTGTTTTGGAAAAAGTTTATTCCTGAATTTGAA  480
    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
421 TATGATGAAATCTACGATCGTGCCAAATTGTTTTGGAAAAAGTTTATTCCTGAATTTGAA  480

481 AAGAAATTCCCCGAAATTAAAAATGTGTTGATAGTTACACATGCAGCAACGAAAATTGCT  540
    ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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            o         o         o         o         o         o

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 901 TTTGAA------------------------------------------------------  906

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 906 ------------------------------------------------------------  905

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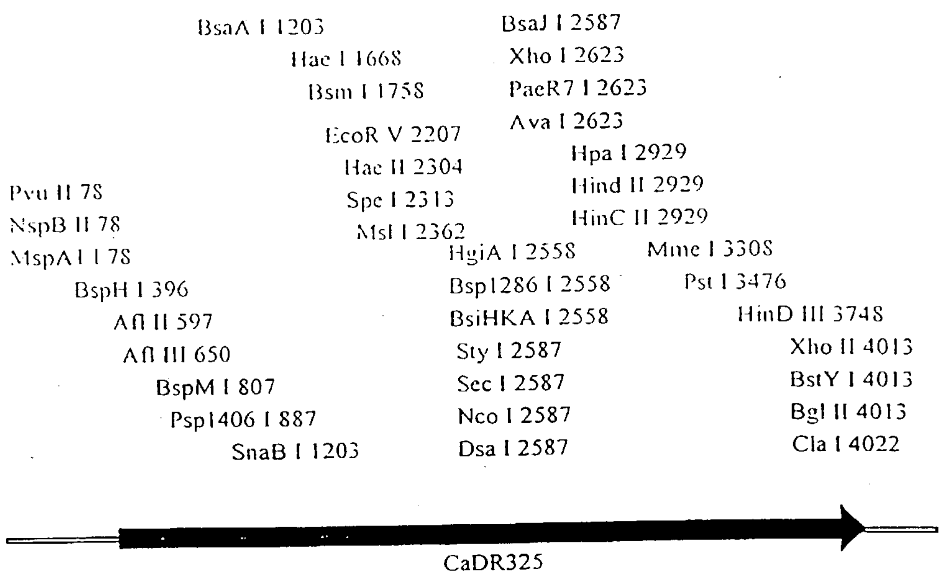
FIG. 7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PaeR7 I 2623
Ava I 2623
Hpa I 2929
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HinC II 2929
Pvu II 78
NspB II 78
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Afl III 650
BspM I 807
Psp1406 I 887
SnaB I 1203
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Bsp1286 I 2558
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Dsa I 2587
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Bgl II 4013
Cla I 4022
CaDR325

Please type a plus sign (+) inside this box → [+]

DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION

[X] Declaration Submitted with Initial Filing OR [ ] Declaration Submitted after Initial Filing

Attorney Docket Number	446.001
First Named Inventor	Jean-Louis LALANNE et al
COMPLETE IF KNOWN	
Application Number	PCT/EP99/07376
Filing Date	September 13, 1999
Group Art Unit	
Examiner Name	

As a below named Inventor, I hereby declare that:

My residence, post office address, and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled :

ESSENTIAL GENES FROM C. ALBICANS AND A METHOD FOR SCREENING ANTIMYCOTIC SUBSTANCES USING SAID GENES

(Title of the Invention)

the specification of which

[ ] is attached hereto

OR

[X] was filed on (MM/DD/YYYY) 09/13/99 as United States Application Number or PCT International

Application Number PCT/EP99/07376 and was amended on (MM/DD/YYYY) ______ (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37 Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code §119 (a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate, or §365 (a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or of any PCT international application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application Number(s)	Country	Foreign Filing Date (MM/DD/YYYY)	Priority Not Claimed	Certified Copy Attached? YES	NO
98402255.8	Europe	09/11/98	[ ]	[ ]	[X]
			[ ]	[ ]	[ ]
			[ ]	[ ]	[ ]
PCT/EP99/07376	PCT	09/13/99	[ ]	[ ]	[ ]
			[ ]	[ ]	[ ]
			[ ]	[ ]	[ ]

[ ] Additional foreign application numbers are listed on a supplemental priority sheet attached hereto:

I hereby claim the benefit under Title 35, United States Code § 119(e) of any United States provisional application(s) listed below.

Application Number(s)	Filing Date (MM/DD/YYYY)	
		[ ] Additional provisional application numbers are listed on a supplemental priority sheet attached hereto.

Please type a plus sign (+) inside this box → [+]

PTO/SB/01 (6-95)
Approved for use through 9/30/98. OMB 0651-0032
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

DECLARATION

I hereby claim the benefit under Title 35, United States Code §120 of any United States application(s), or §365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code §112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

U.S. Parent Application Number	PCT Parent Number	Parent Filing Date (MM/DD/YYYY)	Parent Patent Number *(if applicable)*

☐ Additional U.S. or PCT international application numbers are listed on a supplemental priority sheet attached hereto.

As a named inventor, I hereby appoint the following registered practitioner(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

Name	Registration Number	Name	Registration Number
Bierman, Muserlian and Lucas	18,818		
Jordan B. Bierman	18,629		
Charles A. Muserlian	19,683		
Donald C. Lucas	31,275		

☐ Additional registered practitioner(s) named on a supplemental sheet attached hereto.

Direct all correspondence to:

Name	Charles A. Muserlian				
Address	Bierman, Muserlian and Lucas				
Address	600 Third Avenue				
City	New York	State	NY	ZIP	10016
Country	U.S.A.	Telephone	(212) 661-8000	Fax	(212) 661-8002

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Name of Sole or First Inventor: ☐ A petition has been filed for this unsigned inventor

(W)

Given Name	Jean-Louis	Middle Initial		Family Name	LALANNE	Suffix e.g. Jr.	
Inventor's Signature	FRX				Date	6 March 2001	
Residence: City	Fontenay sous Bois	State		Country	France	Citizenship	France
Post Office Address	110, avenue du Maréchal, F-94120 Fontenay sous Bois, France						
Post Office Address							
City	Fontenay sous Bois	State		Zip	F-94120	Country	France

☒ Additional inventors are being named on supplemental sheet(s) attached hereto

DECLARATION

ADDITIONAL INVENTOR(S)
Supplemental Sheet

2w

Name of Additional Joint Inventor, if any:	☐ A petition has been filed for this unsigned inventor				
Given Name	Corinne	Middle Initial		Family Name	~~ROCHER~~
Suffix e.g. Jr.					
Inventor's Signature	C Rocher	Date	06.02.01		
Residence: City	Paris	State		Country	France FRX
Citizenship	France				
Post Office Address	3, rue Elisa Lemonnier, F-75012 Paris, France				
Post Office Address					
City	Paris	State		Zip	F-75012
Country	France				

3w

Name of Additional Joint Inventor, if any:	☐ A petition has been filed for this unsigned inventor				
Given Name	Thomas	Middle Initial		Family Name	LEEUW
Suffix e.g. Jr.					
Inventor's Signature	X T. L	Date	14.5.01		
Residence: City	Greifenberg	State		Country	Germany DEX
Citizenship	Germany				
Post Office Address	Alspitzweg 11, D-86926 Greifenberg, Germany				
Post Office Address					
City	Greifenberg	State		Zip	D-86926
Country	Germany				

4w

Name of Additional Joint Inventor, if any:	☐ A petition has been filed for this unsigned inventor				
Given Name	Daniel	Middle Initial		Family Name	MARGERIE
Suffix e.g. Jr.					
Inventor's Signature	X D. Margerie	Date	02.05.01		
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Citizenship	Germany				
Post Office Address	Falkstrasse 104, D-60487 Frankfurt am Main, Germany				
Post Office Address					
City	Frankfurt Main	State		Zip	D-60487
Country	Germany				

5w

Name of Additional Joint Inventor, if any:	☐ A petition has been filed for this unsigned inventor				
Given Name	Almut	Middle Initial		Family Name	NITSCHE
Suffix e.g. Jr.					
Inventor's Signature	X A. Nitsche	Date	07.05.01		
Residence: City	Wiesbaden ~~Krailing~~	State		Country	Germany DEX
Citizenship	Germany				
Post Office Address	Emanuel-Geibel-Str. 8 65185 Wiesbaden ~~Bergstrasse 20, D-82152 Krailing~~, Germany				
Post Office Address					
City	Krailing	State		Zip	D-82152
Country	Germany				

☒ Additional inventors are being named on supplemental sheet(s) attached hereto

[redacted]

Please type a plus sign (+) inside this box → [+]

PTO/SB/01 (8-96)
Approved for use through 9/30/98. OMB 0651-0032
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

DECLARATION

ADDITIONAL INVENTOR(S) Supplemental Sheet

Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

Given Name: Jutta | Middle Initial: | Family Name: REINHARD-RUPP | Suffix e.g. Jr.:

6w

Inventor's Signature: X J. Reinhard-Rupp DEX | Date: 03.05.01

Residence: City: ~~München~~ Hofheim | State: | Country: Germany | Citizenship: Germany

Post Office Address: Nussbaumstrasse 25, D-65719 Hofheim, Germany

Post Office Address: ~~Neufriedenheimer Strasse 82A, D-81375, München~~, Germany

City: ~~München~~ Hofheim | State: | Zip: D-~~81375~~ 65719 | Country: Germany

Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

Given Name: Nicolas | Middle Initial: | Family Name: CHALWATZIS | Suffix e.g. Jr.:

7w

Inventor's Signature: X N. Chalwatzis DEX | Date:

Residence: City: Heppenkeim | State: | Country: Germany | Citizenship: Germany

Post Office Address: Krokusweg 15, D-64646 Heppenkeim, Germany

Post Office Address:

City: Heppenkeim | State: | Zip: D-64646 | Country: Germany

Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

Given Name: | Middle Initial: | Family Name: | Suffix e.g. Jr.:

Inventor's Signature: | Date:

Residence: City: | State: | Country: | Citizenship:

Post Office Address:

Post Office Address:

City: | State: | Zip: | Country:

Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

Given Name: | Middle Initial: | Family Name: | Suffix e.g. Jr.:

Inventor's Signature: | Date:

Residence: City: | State: | Country: | Citizenship:

Post Office Address:

Post Office Address:

City: | State: | Zip: | Country:

☐ Additional inventors are being named on supplemental sheet(s) attached hereto

SEQUENCE LISTING

<110> AVENTIS PHARMA S.A.

<120> ESSENTIAL GENES FROM C. ALBICANS AND A METHOD FOR
SCREENING ANTIMYCOTIC SUBSTANCES USING SAID GENES

<130> 16655

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<141> 1999-09-13

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<151> 1998-09-11

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<170> PatentIn Ver. 2.1

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Val Glu Ala Leu Val Ser Lys Ile Gly Gln Leu Thr Phe Gln Lys Tyr
195 200 205

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Asp Ile Ser Met Gly Lys Tyr Asp Glu Lys Ile Phe Asp Val Val Ala
580 585 590

aaa tac gga tgt cct tat atc atg aat cat act cga gga tca cct aaa 1824
Lys Tyr Gly Cys Pro Tyr Ile Met Asn His Thr Arg Gly Ser Pro Lys
595 600 605

acc atg tct aaa ttg acc aat tat gaa tca aat aca aat gat gat att 1872
Thr Met Ser Lys Leu Thr Asn Tyr Glu Ser Asn Thr Asn Asp Asp Ile
610 615 620

atc gaa tat ata att gat cct aaa tta gga cat caa gaa ttg gat ttg 1920
Ile Glu Tyr Ile Ile Asp Pro Lys Leu Gly His Gln Glu Leu Asp Leu
625 630 635 640

tca cct gaa atc aag aat tta ctc aat gga atc agt cgt gaa ttg agt 1968
Ser Pro Glu Ile Lys Asn Leu Leu Asn Gly Ile Ser Arg Glu Leu Ser
645 650 655

tta caa atg ttt aaa gcc atg gct aaa gga gtg aaa aaa tgg caa att 2016
Leu Gln Met Phe Lys Ala Met Ala Lys Gly Val Lys Lys Trp Gln Ile
660 665 670

att ttg gat cct ggt att gga ttt gct aaa aat ttg aat caa aat tta 2064
Ile Leu Asp Pro Gly Ile Gly Phe Ala Lys Asn Leu Asn Gln Asn Leu

675 680 685

gca gtt att cgt aat gcc tcg ttt ttt aaa aaa tat tct att caa att 2112
Ala Val Ile Arg Asn Ala Ser Phe Phe Lys Lys Tyr Ser Ile Gln Ile
690 695 700

aat gaa cgt gtt gat gat gtg aca atc aaa cat aaa tat tta agt ttt 2160
Asn Glu Arg Val Asp Asp Val Thr Ile Lys His Lys Tyr Leu Ser Phe
705 710 715 720

aat ggt gct tgt gtt ttg gtg ggg aca tca aga aag aag ttt ttg ggg 2208
Asn Gly Ala Cys Val Leu Val Gly Thr Ser Arg Lys Lys Phe Leu Gly
725 730 735

aca tta act ggt aat gaa gtg cct ctg gat cga gta ttt ggc act ggt 2256
Thr Leu Thr Gly Asn Glu Val Pro Leu Asp Arg Val Phe Gly Thr Gly
740 745 750

gca aca gtg tct gcg tgt att gaa caa aac act gat att gta aga gtt 2304
Ala Thr Val Ser Ala Cys Ile Glu Gln Asn Thr Asp Ile Val Arg Val
755 760 765

cat gat gtt aaa gaa atg aaa gat gta gta tgt ata agt gat gca att 2352
His Asp Val Lys Glu Met Lys Asp Val Val Cys Ile Ser Asp Ala Ile
770 775 780

tat aaa aat gta taa 2367
Tyr Lys Asn Val
785

<210> 3
<211> 788
<212> PRT
<213> Candida albicans

<400> 3
Met Leu Lys Asn Asp Thr Val Phe Thr Lys Asp Ile Ser Cys Thr Ala
1 5 10 15

Ile Thr Gly Lys Asp Ala Trp Asn Arg Pro Thr Pro Gln Pro Ile Thr
20 25 30

Ile Ser Leu Ser Phe Asn Thr Asp Phe His Lys Ala Ser Glu Leu Asp
35 40 45

Asn Leu Lys Tyr Ser Ile Asn Tyr Ala Val Ile Thr Arg Asn Val Thr
50 55 60

Glu Phe Met Lys Ser Asn Glu His Leu Asn Phe Lys Ser Leu Gly Asn
65 70 75 80

Ile Ala Gln Ala Ile Ser Asp Ile Gly Leu Asp Gln Ser Arg Gly Gly
85 90 95

Gly Ser Ile Val Asp Val Thr Ile Lys Ser Leu Lys Ser Glu Ile Arg
100 105 110

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Ala Glu Ser Val Glu Tyr Lys Ile Asn Arg Asn Thr Leu Gly Gln Pro
        115                 120                 125

Val Pro Leu Asp Ile Phe Gln Val Asn Lys Leu Arg Leu Leu Thr Ile
    130                 135                 140

Ile Gly Val Phe Thr Phe Glu Arg Leu Gln Lys Gln Ile Val Asp Val
145                 150                 155                 160

Asp Leu Gln Phe Lys Ile Glu Pro Asn Ser Asn Leu Tyr Phe His Gln
                165                 170                 175

Ile Ile Ala Asp Ile Val Ser Tyr Val Glu Ser Ser Asn Phe Lys Thr
            180                 185                 190

Val Glu Ala Leu Val Ser Lys Ile Gly Gln Leu Thr Phe Gln Lys Tyr
        195                 200                 205

Asp Gly Val Ala Glu Val Val Ala Thr Val Thr Lys Pro Asn Ala Phe
    210                 215                 220

Ser His Val Glu Gly Val Gly Val Ser Ser Thr Met Val Lys Asp Asn
225                 230                 235                 240

Phe Lys Asp Met Glu Pro Val Lys Phe Glu Asn Thr Ile Ala Gln Thr
                245                 250                 255

Asn Arg Ala Phe Asn Leu Pro Val Glu Asn Glu Lys Thr Glu Asp Tyr
            260                 265                 270

Thr Gly Tyr His Thr Ala Phe Ile Ala Phe Gly Ser Asn Thr Gly Asn
        275                 280                 285

Gln Val Glu Asn Ile Thr Asn Ser Phe Glu Leu Leu Gln Lys Tyr Gly
    290                 295                 300

Ile Thr Ile Glu Ala Thr Ser Ser Leu Tyr Ile Ser Lys Pro Met Tyr
305                 310                 315                 320

Tyr Leu Asp Gln Pro Asp Phe Phe Asn Gly Val Ile Lys Val Asn Phe
                325                 330                 335

Gln Asn Ile Ser Pro Phe Gln Leu Leu Lys Ile Leu Lys Asp Ile Glu
            340                 345                 350

Tyr Lys His Leu Glu Arg Lys Lys Asp Phe Asp Asn Gly Pro Arg Ser
        355                 360                 365

Ile Asp Leu Asp Ile Ile Leu Tyr Asp Asp Leu Gln Leu Asn Thr Glu
    370                 375                 380

Asn Leu Ile Ile Pro His Lys Ser Met Leu Glu Arg Thr Phe Val Leu
385                 390                 395                 400

Gln Pro Leu Cys Glu Val Leu Pro Pro Asp Tyr Ile His Pro Ile Ser
                405                 410                 415
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09786880 .060101

Ala Glu Ser Leu His Ser His Leu Gln Gln Leu Ile Asn Asp Lys Pro
420 425 430

Gln Glu Thr Val Gln Glu Ser Ser Asp Leu Leu Gln Phe Ile Pro Val
435 440 445

Ser Arg Leu Pro Val Lys Asp Asn Ile Leu Lys Phe Asp Gln Ile Asn
450 455 460

His Lys Ser Pro Thr Leu Ile Met Gly Ile Leu Asn Met Thr Pro Asp
465 470 475 480

Ser Phe Ser Asp Gly Gly Lys His Phe Gly Lys Glu Leu Asp Asn Thr
485 490 495

Val Lys Gln Ala Glu Lys Leu Val Ser Glu Gly Ala Thr Ile Ile Asp
500 505 510

Ile Gly Gly Val Ser Thr Arg Pro Gly Ser Val Glu Pro Thr Glu Glu
515 520 525

Glu Glu Leu Glu Arg Val Ile Pro Leu Ile Lys Ala Ile Arg Gln Ser
530 535 540

Leu Asn Pro Asp Leu Leu Lys Val Leu Ile Ser Val Asp Thr Tyr Arg
545 550 555 560

Arg Asn Val Ala Glu Gln Ser Leu Leu Val Gly Ala Asp Ile Ile Asn
565 570 575

Asp Ile Ser Met Gly Lys Tyr Asp Glu Lys Ile Phe Asp Val Val Ala
580 585 590

Lys Tyr Gly Cys Pro Tyr Ile Met Asn His Thr Arg Gly Ser Pro Lys
595 600 605

Thr Met Ser Lys Leu Thr Asn Tyr Glu Ser Asn Thr Asn Asp Asp Ile
610 615 620

Ile Glu Tyr Ile Ile Asp Pro Lys Leu Gly His Gln Glu Leu Asp Leu
625 630 635 640

Ser Pro Glu Ile Lys Asn Leu Leu Asn Gly Ile Ser Arg Glu Leu Ser
645 650 655

Leu Gln Met Phe Lys Ala Met Ala Lys Gly Val Lys Lys Trp Gln Ile
660 665 670

Ile Leu Asp Pro Gly Ile Gly Phe Ala Lys Asn Leu Asn Gln Asn Leu
675 680 685

Ala Val Ile Arg Asn Ala Ser Phe Phe Lys Lys Tyr Ser Ile Gln Ile
690 695 700

Asn Glu Arg Val Asp Asp Val Thr Ile Lys His Lys Tyr Leu Ser Phe
705 710 715 720

Asn Gly Ala Cys Val Leu Val Gly Thr Ser Arg Lys Lys Phe Leu Gly
725 730 735

Thr Leu Thr Gly Asn Glu Val Pro Leu Asp Arg Val Phe Gly Thr Gly
740 745 750

Ala Thr Val Ser Ala Cys Ile Glu Gln Asn Thr Asp Ile Val Arg Val
755 760 765

His Asp Val Lys Glu Met Lys Asp Val Val Cys Ile Ser Asp Ala Ile
770 775 780

Tyr Lys Asn Val
785

<210> 4
<211> 647
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Probe

<400> 4
agtattcaat tgggtattcc cagtaataaa aagaaagatc gatcatcaat tatggtgctt 60

aaaaaaatgt gggattctca attacaatca ttatttaaac atgttgacgg tgcatcaaaa 120

tttgtgcaac cattacccaa tagacacatt gtcgcggaaa gtggacgatg gtttgaagtt 180

aatgtgggga attggaaacc aagttatcca actcatttat ttatatttaa tgatttaatt 240

ttaattgccg ttaaaaaatc atcatctagt agtcaggaac ctactacagg gggaagtaat 300

ggtggttcaa aatcgagatt acaagcggtt caatgttggc ccttaactca agtatcatta 360

caacaaatca aatcaccgaa aaaagatgac gataagatgt attttatcaa tcttaaatcc 420

aaatctttaa gttatgtata cctgacggat cgttatgatc attttgtgaa agttacggaa 480

gcatttaata aaggtagaaa tgaaatgatt caaagtgaaa gattattaga ttcaagactt 540

tcatctcctt caaataataa tggagattct aaagaagaga aacgacaatt acgggaatca 600

ttaagaaact caggcaatta taaagaagga gttactgatg atgccgg 647

<210> 5
<211> 2373
<212> DNA
<213> Candida albicans

<220>
<221> CDS
<222> (1)..(2373)

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<220>
<221> gene
<222> (1)..(2373)
<223> gene CaBR102

<400> 5
atg gat aat ctt gat ccc aat tct agt tta caa gta gag aaa tta cga     48
Met Asp Asn Leu Asp Pro Asn Ser Ser Leu Gln Val Glu Lys Leu Arg
 1               5                  10                  15

aac agg aaa agc agg gct gta tgg cag aat aac aac act tct act cat     96
Asn Arg Lys Ser Arg Ala Val Trp Gln Asn Asn Asn Thr Ser Thr His
            20                  25                  30

aat aat cct tat gct aat tta agc act ggt gaa aaa agt agg agt cgc    144
Asn Asn Pro Tyr Ala Asn Leu Ser Thr Gly Glu Lys Ser Arg Ser Arg
        35                  40                  45

cat aac act ggt agt tct tat gtt tct cca tat ggc ggc ggt aat gga    192
His Asn Thr Gly Ser Ser Tyr Val Ser Pro Tyr Gly Gly Gly Asn Gly
    50                  55                  60

gag gag aat gct tat act ggg aat aac aac aaa tca aat act agt ggt    240
Glu Glu Asn Ala Tyr Thr Gly Asn Asn Asn Lys Ser Asn Thr Ser Gly
65                  70                  75                  80

aat tta tta caa gtt cct gga gca gga gga gga gga gat ttg aat tct    288
Asn Leu Leu Gln Val Pro Gly Ala Gly Gly Gly Gly Asp Leu Asn Ser
                85                  90                  95

aat aag aaa caa agt cga aga atg agt att cat gta tca gct cgt caa    336
Asn Lys Lys Gln Ser Arg Arg Met Ser Ile His Val Ser Ala Arg Gln
            100                 105                 110

cat gga aga tca ttt tca caa act ggt cca att gat atg gca aat tta    384
His Gly Arg Ser Phe Ser Gln Thr Gly Pro Ile Asp Met Ala Asn Leu
        115                 120                 125

ccg gca tta cct aaa ata ggt ggt gtt act act agt ggt gtt ggc ggt    432
Pro Ala Leu Pro Lys Ile Gly Gly Val Thr Thr Ser Gly Val Gly Gly
    130                 135                 140

gct ggt ggt gat gtt atg aca agg act ggg gga ttg acg ata gaa caa    480
Ala Gly Gly Asp Val Met Thr Arg Thr Gly Gly Leu Thr Ile Glu Gln
145                 150                 155                 160

aaa ata ttc aaa gaa tta agt caa gga tca gca gct gaa gtt gat gat    528
Lys Ile Phe Lys Glu Leu Ser Gln Gly Ser Ala Ala Glu Val Asp Asp
                165                 170                 175

tat tac aag aca tta ttg aaa cag aaa aat tta atc act cgt gac att    576
Tyr Tyr Lys Thr Leu Leu Lys Gln Lys Asn Leu Ile Thr Arg Asp Ile
            180                 185                 190

aag gat aat att aat cag aat caa aaa aat att tta caa tta aca aaa    624
Lys Asp Asn Ile Asn Gln Asn Gln Lys Asn Ile Leu Gln Leu Thr Lys
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195 200 205

gac ttg aaa gag acc caa gaa gaa ttg att gaa ttg aga gga acc act 672
Asp Leu Lys Glu Thr Gln Glu Glu Leu Ile Glu Leu Arg Gly Thr Thr
210 215 220

aaa gaa tta tat gaa gtt tta ggt tat ttc aaa gaa tca gct caa cgt 720
Lys Glu Leu Tyr Glu Val Leu Gly Tyr Phe Lys Glu Ser Ala Gln Arg
225 230 235 240

aga tta gaa ttg gaa ttt gaa cca gaa aca caa aaa gaa ctt cat ctg 768
Arg Leu Glu Leu Glu Phe Glu Pro Glu Thr Gln Lys Glu Leu His Leu
245 250 255

cct caa aaa agt aat caa ttg ggt att cct agt aat aaa aag aaa gat 816
Pro Gln Lys Ser Asn Gln Leu Gly Ile Pro Ser Asn Lys Lys Lys Asp
260 265 270

cga tca tca att atg gtg ctt aaa aaa atg tgg gat tct caa tta caa 864
Arg Ser Ser Ile Met Val Leu Lys Lys Met Trp Asp Ser Gln Leu Gln
275 280 285

tca tta ttt aaa cat gtt gac ggt gca tca aaa ttt gtc caa cca tta 912
Ser Leu Phe Lys His Val Asp Gly Ala Ser Lys Phe Val Gln Pro Leu
290 295 300

ccc aat aga cac att gtc gcg gaa agt gga cga tgg ttt gaa gtt aat 960
Pro Asn Arg His Ile Val Ala Glu Ser Gly Arg Trp Phe Glu Val Asn
305 310 315 320

gtg ggg aat tgg aaa cca agt tat cca act cat tta ttt ata ttt aat 1008
Val Gly Asn Trp Lys Pro Ser Tyr Pro Thr His Leu Phe Ile Phe Asn
325 330 335

gat tta att tta att act gtt aaa aaa tca tca tct agt agt cag gaa 1056
Asp Leu Ile Leu Ile Thr Val Lys Lys Ser Ser Ser Ser Ser Gln Glu
340 345 350

cct act aca ggg gga agt aat ggt ggt tca aaa tcg aga tta caa gcg 1104
Pro Thr Thr Gly Gly Ser Asn Gly Gly Ser Lys Ser Arg Leu Gln Ala
355 360 365

gtt caa tgt tgg ccc tta act caa gta tca tta caa caa atc aaa tca 1152
Val Gln Cys Trp Pro Leu Thr Gln Val Ser Leu Gln Gln Ile Lys Ser
370 375 380

ccg aaa aaa gat gac gat aag atg tat ttt atc aat ctt aaa tcc aaa 1200
Pro Lys Lys Asp Asp Asp Lys Met Tyr Phe Ile Asn Leu Lys Ser Lys
385 390 395 400

tct tta agt tat gta tac ctg acg gat cgt tat gat cat ttt gtg aaa 1248
Ser Leu Ser Tyr Val Tyr Leu Thr Asp Arg Tyr Asp His Phe Val Lys
405 410 415

gtt acg gaa gca ttt aat aaa ggt aga aat gaa atg att caa agt gaa 1296
Val Thr Glu Ala Phe Asn Lys Gly Arg Asn Glu Met Ile Gln Ser Glu
420 425 430

aga tta tta gat tca aga ctt tca tct cct tca aat aat aat gga gat 1344
Arg Leu Leu Asp Ser Arg Leu Ser Ser Pro Ser Asn Asn Asn Gly Asp
435 440 445

tct aaa gaa gag aaa cga caa tta cgg gaa tca tta aga aac tca ggc 1392
Ser Lys Glu Glu Lys Arg Gln Leu Arg Glu Ser Leu Arg Asn Ser Gly
450 455 460

aat tat aaa gaa gga gtt act gat gat gcc ggt gga gct gca act ggt 1440
Asn Tyr Lys Glu Gly Val Thr Asp Asp Ala Gly Gly Ala Ala Thr Gly
465 470 475 480

ggt ggt agg aaa agt gcc ggt act cct aat aga aat agt act gat tac 1488
Gly Gly Arg Lys Ser Ala Gly Thr Pro Asn Arg Asn Ser Thr Asp Tyr
485 490 495

gtt tta cat gat ata tct gct cga gta cat tca cgt aat cga tca caa 1536
Val Leu His Asp Ile Ser Ala Arg Val His Ser Arg Asn Arg Ser Gln
500 505 510

gat tta ggg aat aat ttc aaa tta gct aat aat ggg aaa tca caa ttt 1584
Asp Leu Gly Asn Asn Phe Lys Leu Ala Asn Asn Gly Lys Ser Gln Phe
515 520 525

ttc aat gaa atc aaa act tta gaa gat cga tta gat gat gtt gac gtt 1632
Phe Asn Glu Ile Lys Thr Leu Glu Asp Arg Leu Asp Asp Val Asp Val
530 535 540

gaa ata tcg cat aat caa tat gct gaa gcc gtg gaa tta ata tca ata 1680
Glu Ile Ser His Asn Gln Tyr Ala Glu Ala Val Glu Leu Ile Ser Ile
545 550 555 560

att gaa tct aaa tta cgt aat att gaa aat gca tta act aat caa cgt 1728
Ile Glu Ser Lys Leu Arg Asn Ile Glu Asn Ala Leu Thr Asn Gln Arg
565 570 575

aat gga ggt aaa aat gtc aat att gct gat gaa tta tta ctt tta gat 1776
Asn Gly Gly Lys Asn Val Asn Ile Ala Asp Glu Leu Leu Leu Leu Asp
580 585 590

gta tca aaa ttg aaa att aaa aat cgg aaa gaa aat gta tct aat gga 1824
Val Ser Lys Leu Lys Ile Lys Asn Arg Lys Glu Asn Val Ser Asn Gly
595 600 605

tta ata ttt gat tta caa cat aat ata gct aaa ctt aaa caa gat gat 1872
Leu Ile Phe Asp Leu Gln His Asn Ile Ala Lys Leu Lys Gln Asp Asp
610 615 620

att gat aat att ttg acg tta ttt gat aat tta gag caa tta gat cga 1920
Ile Asp Asn Ile Leu Thr Leu Phe Asp Asn Leu Glu Gln Leu Asp Arg
625 630 635 640

ggg gtt caa gga tat ttg gat tca atg tca gct tat tta tca act aca 1968
Gly Val Gln Gly Tyr Leu Asp Ser Met Ser Ala Tyr Leu Ser Thr Thr
645 650 655

gta tca aaa tta att gtt ggt tta caa gga tca acg aaa atc gat gtt 2016
Val Ser Lys Leu Ile Val Gly Leu Gln Gly Ser Thr Lys Ile Asp Val
660 665 670

gtt aat tat ctt tcc aat tta atg gtt att aat gta tcg att gtg aaa 2064
Val Asn Tyr Leu Ser Asn Leu Met Val Ile Asn Val Ser Ile Val Lys
675 680 685

cgt aca att caa act tat gaa caa ata att gct cca att tta aaa cgt 2112
Arg Thr Ile Gln Thr Tyr Glu Gln Ile Ile Ala Pro Ile Leu Lys Arg
690 695 700

cat ggt gat gtt gat tca agt gga ttg att aat tgg tgt att gat gaa 2160
His Gly Asp Val Asp Ser Ser Gly Leu Ile Asn Trp Cys Ile Asp Glu
705 710 715 720

ttt act aaa ctt tgt aaa caa att aaa aaa cat ttg tat gga aca ttg 2208
Phe Thr Lys Leu Cys Lys Gln Ile Lys Lys His Leu Tyr Gly Thr Leu
725 730 735

ttg ata tct tct ggg att aat atg gaa act gat gaa cca att tat aaa 2256
Leu Ile Ser Ser Gly Ile Asn Met Glu Thr Asp Glu Pro Ile Tyr Lys
740 745 750

gtt aaa gaa aga aaa tta tat gat aat ttc ttg aag att atg caa cca 2304
Val Lys Glu Arg Lys Leu Tyr Asp Asn Phe Leu Lys Ile Met Gln Pro
755 760 765

caa ttg gaa gaa tta aaa ctg gtg gga tta aat gtt gat tat ata ttt 2352
Gln Leu Glu Glu Leu Lys Leu Val Gly Leu Asn Val Asp Tyr Ile Phe
770 775 780

gag tct ata tta aat ctt gaa 2373
Glu Ser Ile Leu Asn Leu Glu
785 790

<210> 6
<211> 791
<212> PRT
<213> Candida albicans

<400> 6
Met Asp Asn Leu Asp Pro Asn Ser Ser Leu Gln Val Glu Lys Leu Arg
1 5 10 15

Asn Arg Lys Ser Arg Ala Val Trp Gln Asn Asn Asn Thr Ser Thr His
20 25 30

Asn Asn Pro Tyr Ala Asn Leu Ser Thr Gly Glu Lys Ser Arg Ser Arg
35 40 45

His Asn Thr Gly Ser Ser Tyr Val Ser Pro Tyr Gly Gly Gly Asn Gly
50 55 60

Glu Glu Asn Ala Tyr Thr Gly Asn Asn Asn Lys Ser Asn Thr Ser Gly
65 70 75 80

Asn Leu Leu Gln Val Pro Gly Ala Gly Gly Gly Gly Asp Leu Asn Ser
85 90 95

Asn Lys Lys Gln Ser Arg Arg Met Ser Ile His Val Ser Ala Arg Gln
100 105 110

His Gly Arg Ser Phe Ser Gln Thr Gly Pro Ile Asp Met Ala Asn Leu
115 120 125

Pro Ala Leu Pro Lys Ile Gly Gly Val Thr Thr Ser Gly Val Gly Gly
130 135 140

Ala Gly Gly Asp Val Met Thr Arg Thr Gly Gly Leu Thr Ile Glu Gln
145 150 155 160

Lys Ile Phe Lys Glu Leu Ser Gln Gly Ser Ala Ala Glu Val Asp Asp
165 170 175

Tyr Tyr Lys Thr Leu Leu Lys Gln Lys Asn Leu Ile Thr Arg Asp Ile
180 185 190

Lys Asp Asn Ile Asn Gln Asn Gln Lys Asn Ile Leu Gln Leu Thr Lys
195 200 205

Asp Leu Lys Glu Thr Gln Glu Glu Leu Ile Glu Leu Arg Gly Thr Thr
210 215 220

Lys Glu Leu Tyr Glu Val Leu Gly Tyr Phe Lys Glu Ser Ala Gln Arg
225 230 235 240

Arg Leu Glu Leu Glu Phe Glu Pro Glu Thr Gln Lys Glu Leu His Leu
245 250 255

Pro Gln Lys Ser Asn Gln Leu Gly Ile Pro Ser Asn Lys Lys Lys Asp
260 265 270

Arg Ser Ser Ile Met Val Leu Lys Lys Met Trp Asp Ser Gln Leu Gln
275 280 285

Ser Leu Phe Lys His Val Asp Gly Ala Ser Lys Phe Val Gln Pro Leu
290 295 300

Pro Asn Arg His Ile Val Ala Glu Ser Gly Arg Trp Phe Glu Val Asn
305 310 315 320

Val Gly Asn Trp Lys Pro Ser Tyr Pro Thr His Leu Phe Ile Phe Asn
325 330 335

Asp Leu Ile Leu Ile Thr Val Lys Lys Ser Ser Ser Ser Ser Gln Glu
340 345 350

Pro Thr Thr Gly Gly Ser Asn Gly Gly Ser Lys Ser Arg Leu Gln Ala
355 360 365

Val Gln Cys Trp Pro Leu Thr Gln Val Ser Leu Gln Gln Ile Lys Ser
370 375 380

Pro Lys Lys Asp Asp Asp Lys Met Tyr Phe Ile Asn Leu Lys Ser Lys
385 390 395 400

Ser Leu Ser Tyr Val Tyr Leu Thr Asp Arg Tyr Asp His Phe Val Lys
405 410 415

Val Thr Glu Ala Phe Asn Lys Gly Arg Asn Glu Met Ile Gln Ser Glu
420 425 430

Arg Leu Leu Asp Ser Arg Leu Ser Ser Pro Ser Asn Asn Asn Gly Asp
435 440 445

Ser Lys Glu Glu Lys Arg Gln Leu Arg Glu Ser Leu Arg Asn Ser Gly
450 455 460

Asn Tyr Lys Glu Gly Val Thr Asp Asp Ala Gly Gly Ala Ala Thr Gly
465 470 475 480

Gly Gly Arg Lys Ser Ala Gly Thr Pro Asn Arg Asn Ser Thr Asp Tyr
485 490 495

Val Leu His Asp Ile Ser Ala Arg Val His Ser Arg Asn Arg Ser Gln
500 505 510

Asp Leu Gly Asn Asn Phe Lys Leu Ala Asn Asn Gly Lys Ser Gln Phe
515 520 525

Phe Asn Glu Ile Lys Thr Leu Glu Asp Arg Leu Asp Asp Val Asp Val
530 535 540

Glu Ile Ser His Asn Gln Tyr Ala Glu Ala Val Glu Leu Ile Ser Ile
545 550 555 560

Ile Glu Ser Lys Leu Arg Asn Ile Glu Asn Ala Leu Thr Asn Gln Arg
565 570 575

Asn Gly Gly Lys Asn Val Asn Ile Ala Asp Glu Leu Leu Leu Leu Asp
580 585 590

Val Ser Lys Leu Lys Ile Lys Asn Arg Lys Glu Asn Val Ser Asn Gly
595 600 605

Leu Ile Phe Asp Leu Gln His Asn Ile Ala Lys Leu Lys Gln Asp Asp
610 615 620

Ile Asp Asn Ile Leu Thr Leu Phe Asp Asn Leu Glu Gln Leu Asp Arg
625 630 635 640

Gly Val Gln Gly Tyr Leu Asp Ser Met Ser Ala Tyr Leu Ser Thr Thr
645 650 655

Val Ser Lys Leu Ile Val Gly Leu Gln Gly Ser Thr Lys Ile Asp Val
660 665 670

Val Asn Tyr Leu Ser Asn Leu Met Val Ile Asn Val Ser Ile Val Lys
675 680 685

Arg Thr Ile Gln Thr Tyr Glu Gln Ile Ile Ala Pro Ile Leu Lys Arg
    690   695   700

His Gly Asp Val Asp Ser Ser Gly Leu Ile Asn Trp Cys Ile Asp Glu
705   710   715   720

Phe Thr Lys Leu Cys Lys Gln Ile Lys Lys His Leu Tyr Gly Thr Leu
                725   730   735

Leu Ile Ser Ser Gly Ile Asn Met Glu Thr Asp Glu Pro Ile Tyr Lys
            740   745   750

Val Lys Glu Arg Lys Leu Tyr Asp Asn Phe Leu Lys Ile Met Gln Pro
        755   760   765

Gln Leu Glu Glu Leu Lys Leu Val Gly Leu Asn Val Asp Tyr Ile Phe
    770   775   780

Glu Ser Ile Leu Asn Leu Glu
785   790

<210> 7
<211> 343
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Probe

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ctgcagtaaa ccctccagat ataacagact ctttatgtcc agtgatttcg ccaacaaatc 60

ttggtggttg ggtgtgtgtg gtccataagt atgccgtgtt gtcaccaccc ccagtcaata 120

ccattggcaa tttaggatgt gaaaaaatag taaatatact atcggtatgt ttatcaaaat 180

aagtccatga attgttggac atgtcaattt ctaaagtctc atgctcatca tctaattcca 240

tctcctcatc ttcttcatcg ggtggcgctt gatcatcatc tgcaacttcc tcagccactt 300

cattaacatt gatatattct tcttgagtat cgtctacgac gtc 343

<210> 8
<211> 1248
<212> DNA
<213> Candida albicans

<220>
<221> CDS
<222> (1)..(1245)

<220>
<221> gene
<222> (1)..(1245)

<223> gene CaIR012

<400> 8

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Met Ser His Gln Gln Glu Asp Val Val Asp Asp Thr Gln Glu Glu Tyr
 1               5                  10                  15

atc aat gtt aat gaa gtg gct gag gaa gtt gca gat gat gat caa gcg      96
Ile Asn Val Asn Glu Val Ala Glu Glu Val Ala Asp Asp Asp Gln Ala
            20                  25                  30

cca ccc gat gaa gaa gat gag gag atg gaa tta gat gat gag cat gag     144
Pro Pro Asp Glu Glu Asp Glu Glu Met Glu Leu Asp Asp Glu His Glu
        35                  40                  45

act tta gaa att gac atg tcc aac aat tca tgg act tat ttt gat aaa     192
Thr Leu Glu Ile Asp Met Ser Asn Asn Ser Trp Thr Tyr Phe Asp Lys
    50                  55                  60

cat acc gat agt ata ttt act att ttt tca cat cct aaa ttg cca atg     240
His Thr Asp Ser Ile Phe Thr Ile Phe Ser His Pro Lys Leu Pro Met
65                  70                  75                  80

gta ttg act ggg ggt ggt gac aac acg gca tac tta tgg acc aca cac     288
Val Leu Thr Gly Gly Gly Asp Asn Thr Ala Tyr Leu Trp Thr Thr His
                85                  90                  95

acc caa cca cca aga ttt gtt ggc gaa atc act gga cat aaa gag tct     336
Thr Gln Pro Pro Arg Phe Val Gly Glu Ile Thr Gly His Lys Glu Ser
            100                 105                 110

gtt ata tct gga ggg ttt act gca gac ggc aag ttt gtt gtt act gca     384
Val Ile Ser Gly Gly Phe Thr Ala Asp Gly Lys Phe Val Val Thr Ala
        115                 120                 125

gac atg aat gga tta att caa gtt ttc aaa gcc aca aaa gga ggt gaa     432
Asp Met Asn Gly Leu Ile Gln Val Phe Lys Ala Thr Lys Gly Gly Glu
    130                 135                 140

cag tgg gtg aaa ttt ggt gaa ttg gac gaa gtt gaa gaa gtg ttg ttt     480
Gln Trp Val Lys Phe Gly Glu Leu Asp Glu Val Glu Glu Val Leu Phe
145                 150                 155                 160

gtt act gtg cat cca aca tta cca ttc ttt gcc ttt ggt gct acc gat     528
Val Thr Val His Pro Thr Leu Pro Phe Phe Ala Phe Gly Ala Thr Asp
                165                 170                 175

gga tct ata tgg gtc tac caa ata gac gaa tcc agt aaa ctg cta gtg     576
Gly Ser Ile Trp Val Tyr Gln Ile Asp Glu Ser Ser Lys Leu Leu Val
            180                 185                 190

caa att atg tct ggg ttc tca cac aca tta gaa tgt aat ggt gct gta     624
Gln Ile Met Ser Gly Phe Ser His Thr Leu Glu Cys Asn Gly Ala Val
        195                 200                 205

ttt ata caa gga aaa gat gaa aat gat ttg aca ttg gtc tct ata agt     672
Phe Ile Gln Gly Lys Asp Glu Asn Asp Leu Thr Leu Val Ser Ile Ser
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210 215 220

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gaa gat ggt act gtg gtg aac tgg aac tgt ttt aca gga caa gtg aat     720
Glu Asp Gly Thr Val Val Asn Trp Asn Cys Phe Thr Gly Gln Val Asn
225                 230                 235                 240

tat aaa ttg caa cct cat gat gac ttt aaa gga gtt gaa agt ccg tgg     768
Tyr Lys Leu Gln Pro His Asp Asp Phe Lys Gly Val Glu Ser Pro Trp
                245                 250                 255

gtc acg gtc aaa gta cat ggt aat ctt gtg gcc att ggt ggc aga gat     816
Val Thr Val Lys Val His Gly Asn Leu Val Ala Ile Gly Gly Arg Asp
            260                 265                 270

ggc cag cta tca att gtg aac aat gac act ggt aaa atc gtt cat act     864
Gly Gln Leu Ser Ile Val Asn Asn Asp Thr Gly Lys Ile Val His Thr
        275                 280                 285

ctt aaa aca ttg gat aat gtc gac gac att gca gaa ctc tca att gag     912
Leu Lys Thr Leu Asp Asn Val Asp Asp Ile Ala Glu Leu Ser Ile Glu
    290                 295                 300

gca ttg agt tgg tgt gaa agc aaa aat att aac ctc ttg gca gtg ggt     960
Ala Leu Ser Trp Cys Glu Ser Lys Asn Ile Asn Leu Leu Ala Val Gly
305                 310                 315                 320

ttg gtt tct ggt gac gtt tta tta ttt gat act cag caa tgg aga ttg    1008
Leu Val Ser Gly Asp Val Leu Leu Phe Asp Thr Gln Gln Trp Arg Leu
                325                 330                 335

aga aag aac ttg aaa gtt gac gat gcc atc acc aaa tta caa ttt gtt    1056
Arg Lys Asn Leu Lys Val Asp Asp Ala Ile Thr Lys Leu Gln Phe Val
            340                 345                 350

ggc gaa acc ccc att ttg gtg gga agt agt atg gat ggt aaa att tac    1104
Gly Glu Thr Pro Ile Leu Val Gly Ser Ser Met Asp Gly Lys Ile Tyr
        355                 360                 365

aaa tgg gac gct aga act ggt gaa gag ttg ttt gct ggt gtg gga cac    1152
Lys Trp Asp Ala Arg Thr Gly Glu Glu Leu Phe Ala Gly Val Gly His
    370                 375                 380

aac atg gga gta ttg gac ttt gct att tta gat gga ggt aaa aag ttg    1200
Asn Met Gly Val Leu Asp Phe Ala Ile Leu Asp Gly Gly Lys Lys Leu
385                 390                 395                 400

gtt act gct ggt gat gaa ggt gtt tca ttg gtc ttt gta cat gaa tag    1248
Val Thr Ala Gly Asp Glu Gly Val Ser Leu Val Phe Val His Glu
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Pro Pro Asp Glu Glu Asp Glu Glu Met Glu Leu Asp Asp Glu His Glu
        35                  40                  45

Thr Leu Glu Ile Asp Met Ser Asn Asn Ser Trp Thr Tyr Phe Asp Lys
    50                  55                  60

His Thr Asp Ser Ile Phe Thr Ile Phe Ser His Pro Lys Leu Pro Met
65                  70                  75                      80

Val Leu Thr Gly Gly Gly Asp Asn Thr Ala Tyr Leu Trp Thr Thr His
                85                  90                  95

Thr Gln Pro Pro Arg Phe Val Gly Glu Ile Thr Gly His Lys Glu Ser
            100                 105                 110

Val Ile Ser Gly Gly Phe Thr Ala Asp Gly Lys Phe Val Val Thr Ala
        115                 120                 125

Asp Met Asn Gly Leu Ile Gln Val Phe Lys Ala Thr Lys Gly Gly Glu
    130                 135                 140

Gln Trp Val Lys Phe Gly Glu Leu Asp Glu Val Glu Glu Val Leu Phe
145                 150                 155                 160

Val Thr Val His Pro Thr Leu Pro Phe Phe Ala Phe Gly Ala Thr Asp
                165                 170                 175

Gly Ser Ile Trp Val Tyr Gln Ile Asp Glu Ser Ser Lys Leu Leu Val
            180                 185                 190

Gln Ile Met Ser Gly Phe Ser His Thr Leu Glu Cys Asn Gly Ala Val
        195                 200                 205

Phe Ile Gln Gly Lys Asp Glu Asn Asp Leu Thr Leu Val Ser Ile Ser
    210                 215                 220

Glu Asp Gly Thr Val Val Asn Trp Asn Cys Phe Thr Gly Gln Val Asn
225                 230                 235                 240

Tyr Lys Leu Gln Pro His Asp Asp Phe Lys Gly Val Glu Ser Pro Trp
                245                 250                 255

Val Thr Val Lys Val His Gly Asn Leu Val Ala Ile Gly Gly Arg Asp
            260                 265                 270

Gly Gln Leu Ser Ile Val Asn Asn Asp Thr Gly Lys Ile Val His Thr
        275                 280                 285

Leu Lys Thr Leu Asp Asn Val Asp Asp Ile Ala Glu Leu Ser Ile Glu
    290                 295                 300
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Ala Leu Ser Trp Cys Glu Ser Lys Asn Ile Asn Leu Leu Ala Val Gly
305 310 315 320

Leu Val Ser Gly Asp Val Leu Leu Phe Asp Thr Gln Gln Trp Arg Leu
325 330 335

Arg Lys Asn Leu Lys Val Asp Asp Ala Ile Thr Lys Leu Gln Phe Val
340 345 350

Gly Glu Thr Pro Ile Leu Val Gly Ser Ser Met Asp Gly Lys Ile Tyr
355 360 365

Lys Trp Asp Ala Arg Thr Gly Glu Glu Leu Phe Ala Gly Val Gly His
370 375 380

Asn Met Gly Val Leu Asp Phe Ala Ile Leu Asp Gly Gly Lys Lys Leu
385 390 395 400

Val Thr Ala Gly Asp Glu Gly Val Ser Leu Val Phe Val His Glu
405 410 415

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aac acc ctc aag ttt gag tcc aat ata gat ttg gat aca atc gac ttc 96
Asn Thr Leu Lys Phe Glu Ser Asn Ile Asp Leu Asp Thr Ile Asp Phe
20 25 30

acc agc atc aag aat gat ctt gca aat gtt ttg att aca cca gtc cct 144
Thr Ser Ile Lys Asn Asp Leu Ala Asn Val Leu Ile Thr Pro Val Pro
35 40 45

ctg gat caa tca cgt agc aaa ctt gga gac gca tca aaa cca gtg gcg 192
Leu Asp Gln Ser Arg Ser Lys Leu Gly Asp Ala Ser Lys Pro Val Ala
50 55 60

ttg ccc agt gga gat gag gtg aaa ttg aat caa gca tca att gaa att 240
Leu Pro Ser Gly Asp Glu Val Lys Leu Asn Gln Ala Ser Ile Glu Ile
65 70 75 80

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act gga gtt tta tca aat gaa ttg gat tta gat gaa cta aat aca gca     288
Thr Gly Val Leu Ser Asn Glu Leu Asp Leu Asp Glu Leu Asn Thr Ala
                85                  90                  95

gag ttg tta tat aac gca agt gac ttg agc tac aag aag gga acg tcc     336
Glu Leu Leu Tyr Asn Ala Ser Asp Leu Ser Tyr Lys Lys Gly Thr Ser
            100                 105                 110

att ggc gat agt gct cga ttg gct tat tat tta aga gct cat tat ata     384
Ile Gly Asp Ser Ala Arg Leu Ala Tyr Tyr Leu Arg Ala His Tyr Ile
        115                 120                 125

cta aac att gtt gga tac tta gtt tcg cat aaa cgt tta gat atc atc     432
Leu Asn Ile Val Gly Tyr Leu Val Ser His Lys Arg Leu Asp Ile Ile
    130                 135                 140

act aac aac aac caa gtg ttg ttt gac aat att ttg aaa agt ttc agc     480
Thr Asn Asn Asn Gln Val Leu Phe Asp Asn Ile Leu Lys Ser Phe Ser
145                 150                 155                 160

aag att tat act ttg agt ggt aaa tta aat gac atg att gac aag caa     528
Lys Ile Tyr Thr Leu Ser Gly Lys Leu Asn Asp Met Ile Asp Lys Gln
                165                 170                 175

aaa gtt acc ggc gac atc aac aat ctt gca ttt atc aat tgt atc aat     576
Lys Val Thr Gly Asp Ile Asn Asn Leu Ala Phe Ile Asn Cys Ile Asn
            180                 185                 190

tat tcc aga agt cag ttg ttt aat gca cac gag tta ttg gga caa gtt     624
Tyr Ser Arg Ser Gln Leu Phe Asn Ala His Glu Leu Leu Gly Gln Val
        195                 200                 205

gta ttt gga tta gcg gat aat tat tat gag agt tat ggc aca cta aac     672
Val Phe Gly Leu Ala Asp Asn Tyr Tyr Glu Ser Tyr Gly Thr Leu Asn
    210                 215                 220

aac tat aat tcc tta gtg gag ttt ata ctg aaa aat atc agc gat gaa     720
Asn Tyr Asn Ser Leu Val Glu Phe Ile Leu Lys Asn Ile Ser Asp Glu
225                 230                 235                 240

gat gtt ttt gtt atc cat ttt tta cca tcc act tta caa ttg ttc aag     768
Asp Val Phe Val Ile His Phe Leu Pro Ser Thr Leu Gln Leu Phe Lys
                245                 250                 255

aaa tta ctt caa cta ggt gag gaa tct tta gtc gat cag ttt tac aag     816
Lys Leu Leu Gln Leu Gly Glu Glu Ser Leu Val Asp Gln Phe Tyr Lys
            260                 265                 270

act ata acc tct tcc ata cta aaa gat tat gaa gcc aac aat ttt tcc     864
Thr Ile Thr Ser Ser Ile Leu Lys Asp Tyr Glu Ala Asn Asn Phe Ser
        275                 280                 285

aaa agt gaa gat att gac ttg tca aaa tca aaa ttg tct ggc ttt gaa     912
Lys Ser Glu Asp Ile Asp Leu Ser Lys Ser Lys Leu Ser Gly Phe Glu
    290                 295                 300

ata gtc aca agc ttt att ttt cta act gag ttt att cca tgg tgc aag     960
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Ile Val Thr Ser Phe Ile Phe Leu Thr Glu Phe Ile Pro Trp Cys Lys
305 310 315 320

cag ctg tca agt aga acc gcg aaa tac gat ttc aaa gat gat ata tta 1008
Gln Leu Ser Ser Arg Thr Ala Lys Tyr Asp Phe Lys Asp Asp Ile Leu
325 330 335

aag tat atg gaa ttc ttg ata agt tat gga gtt atg gaa cga tta tta 1056
Lys Tyr Met Glu Phe Leu Ile Ser Tyr Gly Val Met Glu Arg Leu Leu
340 345 350

tca tac tgt tct gaa acc agc aat gca aaa act cag caa gtg tac gac 1104
Ser Tyr Cys Ser Glu Thr Ser Asn Ala Lys Thr Gln Gln Val Tyr Asp
355 360 365

tgg tca aac atg tac gat ttc aga gca ttg ctt caa aag aat ttc cca 1152
Trp Ser Asn Met Tyr Asp Phe Arg Ala Leu Leu Gln Lys Asn Phe Pro
370 375 380

cga ctt aca cca gca aaa ttt cat tat cct ggc aat caa gaa ttg ttg 1200
Arg Leu Thr Pro Ala Lys Phe His Tyr Pro Gly Asn Gln Glu Leu Leu
385 390 395 400

aat gca gtt aga ccg gga tat gaa aat ata tcc aaa ttg att gac att 1248
Asn Ala Val Arg Pro Gly Tyr Glu Asn Ile Ser Lys Leu Ile Asp Ile
405 410 415

tcc ttt ttg acg tta gat cca tcg ctt aat gag acg ttg gtt tca cct 1296
Ser Phe Leu Thr Leu Asp Pro Ser Leu Asn Glu Thr Leu Val Ser Pro
420 425 430

ttt ttc cag agc ttt ttc agt gtg ttt ata tct aat gcc gca gtt gtt 1344
Phe Phe Gln Ser Phe Phe Ser Val Phe Ile Ser Asn Ala Ala Val Val
435 440 445

atg acc tct tta agg gac tca gag gaa gat ttt gtt tta tcg tcg ttg 1392
Met Thr Ser Leu Arg Asp Ser Glu Glu Asp Phe Val Leu Ser Ser Leu
450 455 460

aat gaa agt gac gaa gag gaa gaa gaa gaa gaa agc gac agc gac gaa 1440
Asn Glu Ser Asp Glu Glu Glu Glu Glu Glu Glu Ser Asp Ser Asp Glu
465 470 475 480

gat tct tcg acc cca aaa aac aaa gaa aaa tca gct ggg tta gac ctt 1488
Asp Ser Ser Thr Pro Lys Asn Lys Glu Lys Ser Ala Gly Leu Asp Leu
485 490 495

gac aag att gcc cag cgt gct gaa tta gaa agg ttc tac ttg gct ttc 1536
Asp Lys Ile Ala Gln Arg Ala Glu Leu Glu Arg Phe Tyr Leu Ala Phe
500 505 510

gcg tac acc tac aac aat cga cct gaa ttg tgt gcg tta ttt tgg ggg 1584
Ala Tyr Thr Tyr Asn Asn Arg Pro Glu Leu Cys Ala Leu Phe Trp Gly
515 520 525

aac gag cag gta act cat gac att ata gga ttt att tcc tgg gga ctt 1632
Asn Glu Gln Val Thr His Asp Ile Ile Gly Phe Ile Ser Trp Gly Leu

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530                 535                 540

gct aat aat acg tct ccg ttg atc act gca aca ttc tgc tta cta tta     1680
Ala Asn Asn Thr Ser Pro Leu Ile Thr Ala Thr Phe Cys Leu Leu Leu
545                 550                 555                 560

ggg tcg ttg gca tct gct ggt gca gag gca act tca agg ata tgg gag     1728
Gly Ser Leu Ala Ser Ala Gly Ala Glu Ala Thr Ser Arg Ile Trp Glu
                565                 570                 575

att ctt gta cac aac aat aac aac gca agt acg aga aaa aat gat ttt     1776
Ile Leu Val His Asn Asn Asn Asn Ala Ser Thr Arg Lys Asn Asp Phe
            580                 585                 590

tca aag gta tcc gtt gac tcc ctt tat gat tcg ttg aaa tat tac att     1824
Ser Lys Val Ser Val Asp Ser Leu Tyr Asp Ser Leu Lys Tyr Tyr Ile
        595                 600                 605

gac tct tta aat gaa agc ttt gaa caa gat tta aat gcc caa ttg atg     1872
Asp Ser Leu Asn Glu Ser Phe Glu Gln Asp Leu Asn Ala Gln Leu Met
    610                 615                 620

ttg aat cag aag aaa caa gat ttt ctc ttc agc acc aca aca agc aaa     1920
Leu Asn Gln Lys Lys Gln Asp Phe Leu Phe Ser Thr Thr Thr Ser Lys
625                 630                 635                 640

cag gac ctt gat gat tct ggc gag aat aga att gtt ata gag ttg gcc     1968
Gln Asp Leu Asp Asp Ser Gly Glu Asn Arg Ile Val Ile Glu Leu Ala
                645                 650                 655

gag gat tca ctt gtc ctc att tca ggg ttt att caa tta ctt tct gca     2016
Glu Asp Ser Leu Val Leu Ile Ser Gly Phe Ile Gln Leu Leu Ser Ala
            660                 665                 670

att gtg aag aat ttg aac act aag aat gaa aga agc aaa gaa atc aaa     2064
Ile Val Lys Asn Leu Asn Thr Lys Asn Glu Arg Ser Lys Glu Ile Lys
        675                 680                 685

tcc gtg gta tac act aga ttc tca cca atc att aaa ggg ttt tta aaa     2112
Ser Val Val Tyr Thr Arg Phe Ser Pro Ile Ile Lys Gly Phe Leu Lys
    690                 695                 700

ttc gat aat ttg atc aat ggt agc agg ttc ctt caa gtt gat gct agc     2160
Phe Asp Asn Leu Ile Asn Gly Ser Arg Phe Leu Gln Val Asp Ala Ser
705                 710                 715                 720

att caa agc aca aac aac ccc aaa ttt att gat ttg cca aat gtt ttc     2208
Ile Gln Ser Thr Asn Asn Pro Lys Phe Ile Asp Leu Pro Asn Val Phe
                725                 730                 735

gtc agt gat gac tcg aga att ata ttg acg aac ctc att cta acc ttt     2256
Val Ser Asp Asp Ser Arg Ile Ile Leu Thr Asn Leu Ile Leu Thr Phe
            740                 745                 750

tta ggc gat ttt gtt acc aac gat agt gat ccg tat att aga tat gag     2304
Leu Gly Asp Phe Val Thr Asn Asp Ser Asp Pro Tyr Ile Arg Tyr Glu
        755                 760                 765
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att tgg cgt tta gtc gat cga tgg atg tac cag ggg ttg cat agt ttg 2352
Ile Trp Arg Leu Val Asp Arg Trp Met Tyr Gln Gly Leu His Ser Leu
770 775 780

cca gaa gac aag aaa gat gat gct ttt aga cat att aag aga aag tat 2400
Pro Glu Asp Lys Lys Asp Asp Ala Phe Arg His Ile Lys Arg Lys Tyr
785 790 795 800

aac agt aag aaa aat gtt ccc atc aat caa gca ttt tca aca aac cta 2448
Asn Ser Lys Lys Asn Val Pro Ile Asn Gln Ala Phe Ser Thr Asn Leu
805 810 815

act cat ctt agt caa att ggg aat ttc act gtc ttg gtg aaa aaa ttg 2496
Thr His Leu Ser Gln Ile Gly Asn Phe Thr Val Leu Val Lys Lys Leu
820 825 830

tta acc cca tat gca gat agt aat gaa gca ttc acc aag tac tcg ttg 2544
Leu Thr Pro Tyr Ala Asp Ser Asn Glu Ala Phe Thr Lys Tyr Ser Leu
835 840 845

ttg tat cct tgt gac tta gga tta ggg tat aga ttc aac aac caa ctt 2592
Leu Tyr Pro Cys Asp Leu Gly Leu Gly Tyr Arg Phe Asn Asn Gln Leu
850 855 860

gga att tgg cca tac att gaa ttt tta atg caa aat gtg ttt gca aat 2640
Gly Ile Trp Pro Tyr Ile Glu Phe Leu Met Gln Asn Val Phe Ala Asn
865 870 875 880

tct ggt act att gct aat aaa cga gat agg gtc aac ttg caa ctt aat 2688
Ser Gly Thr Ile Ala Asn Lys Arg Asp Arg Val Asn Leu Gln Leu Asn
885 890 895

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900 905 910

ctt att gat gtg gca ccg aaa att att cgt gac ttg aaa aat ttt aat 2784
Leu Ile Asp Val Ala Pro Lys Ile Ile Arg Asp Leu Lys Asn Phe Asn
915 920 925

ggg ata ttt gac tcg ctt att cct ggt gtt caa ttg gac ttt gaa gtg 2832
Gly Ile Phe Asp Ser Leu Ile Pro Gly Val Gln Leu Asp Phe Glu Val
930 935 940

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Phe Val Lys Leu His His Ser Val Ala Val Ile Asn Tyr Leu Phe Glu
945 950 955 960

aac agg aca ttt tct gcc ttg ttt aag ctt gtt aat att gga gtt gat 2928
Asn Arg Thr Phe Ser Ala Leu Phe Lys Leu Val Asn Ile Gly Val Asp
965 970 975

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Ser Val Asn Glu Ser Gly Glu Ser Ala Glu Leu Val Ser His Ala Leu
980 985 990

ggg ttg att aat tct ttg ttg aga gtt caa aat tct ttt ata aac aag 3024
Gly Leu Ile Asn Ser Leu Leu Arg Val Gln Asn Ser Phe Ile Asn Lys
995 1000 1005

ttg tta cca ata ttg cga aac aaa gat acg cag caa caa tta cat cgt 3072
Leu Leu Pro Ile Leu Arg Asn Lys Asp Thr Gln Gln Gln Leu His Arg
1010 1015 1020

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Gly Thr Ala Ile Gly Ile Gly Thr Ser Met Ser Leu Ala Leu Ala Thr
1025 1030 1035 1040

cct aga acc ata ttt gat tgt ata tac tat cca aag aat ttg gga aca 3168
Pro Arg Thr Ile Phe Asp Cys Ile Tyr Tyr Pro Lys Asn Leu Gly Thr
1045 1050 1055

cat ggt gtt gct gat ttt tac gaa gtg ata ttg ttc cac tta tct gca 3216
His Gly Val Ala Asp Phe Tyr Glu Val Ile Leu Phe His Leu Ser Ala
1060 1065 1070

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Val Val Gln Phe Ala Leu Tyr Val Ser Cys Glu Asn Thr Ile Ser Asn
1075 1080 1085

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Lys Ala Ile Ser Ile Leu Lys Gly Val Ser Gln Ser Lys Phe Phe Val
1090 1095 1100

acc aga gtt tca agc tct gct gat ccc tta ctc aac aac gat aga ttg 3360
Thr Arg Val Ser Ser Ser Ala Asp Pro Leu Leu Asn Asn Asp Arg Leu
1105 1110 1115 1120

att acc aca ttt gaa aac atc gac gag tca ata aaa atc aag ttt gct 3408
Ile Thr Thr Phe Glu Asn Ile Asp Glu Ser Ile Lys Ile Lys Phe Ala
1125 1130 1135

ttc att gac aag ttt gaa gaa ctc gag gac tct ttg aat atg aaa tat 3456
Phe Ile Asp Lys Phe Glu Glu Leu Glu Asp Ser Leu Asn Met Lys Tyr
1140 1145 1150

gag ata ttg gat ttt gtt ttg ggc aat ctc aat caa ttt gat ggc aaa 3504
Glu Ile Leu Asp Phe Val Leu Gly Asn Leu Asn Gln Phe Asp Gly Lys
1155 1160 1165

gtg gct act act gcc cac ttt ttg ttg gga tac aaa gtg aaa ggc gat 3552
Val Ala Thr Thr Ala His Phe Leu Leu Gly Tyr Lys Val Lys Gly Asp
1170 1175 1180

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Thr Leu Asp Leu Val Gln Thr Asn Asp Gln Asn Thr Leu Leu Lys Ser
1185 1190 1195 1200

ttc tta aat aca ttg agc att agt ctt gat ttg att tct gaa att gat 3648
Phe Leu Asn Thr Leu Ser Ile Ser Leu Asp Leu Ile Ser Glu Ile Asp
1205 1210 1215

tac aat aat ggt aat aac cat att att gat gtt ggt cca gcc aag ctt 3696

Tyr Asn Asn Gly Asn Asn His Ile Ile Asp Val Gly Pro Ala Lys Leu
1220 1225 1230

tcg tcg ttg att tta cag att ctt atc aag ttg tgc caa gat cca att 3744
Ser Ser Leu Ile Leu Gln Ile Leu Ile Lys Leu Cys Gln Asp Pro Ile
1235 1240 1245

tcg tcg tca ata aca ttg aat caa tta cgt gaa tat gaa gaa ttg ttt 3792
Ser Ser Ser Ile Thr Leu Asn Gln Leu Arg Glu Tyr Glu Glu Leu Phe
1250 1255 1260

gaa aaa ttg gtt aac tgt caa cct aaa ctt gat ttg aat acc gtt tgg 3840
Glu Lys Leu Val Asn Cys Gln Pro Lys Leu Asp Leu Asn Thr Val Trp
1265 1270 1275 1280

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Cys Gly Asn Gln Phe Asp Gly Asp Leu Gln Ile Asp Ala Ser Asn Val
1285 1290 1295

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1300 1305 1310

cag aga aac tta att ttg cag tat ttg tca ttg gaa ttc cat agt gtc 3984
Gln Arg Asn Leu Ile Leu Gln Tyr Leu Ser Leu Glu Phe His Ser Val
1315 1320 1325

aaa tca aga act aag cgg gag tat tat tct aaa gtg ttg acc aac gac 4032
Lys Ser Arg Thr Lys Arg Glu Tyr Tyr Ser Lys Val Leu Thr Asn Asp
1330 1335 1340

aag gaa ttt gtt aat cgt aca cct aag gtg ttg aca ttt tta aac att 4080
Lys Glu Phe Val Asn Arg Thr Pro Lys Val Leu Thr Phe Leu Asn Ile
1345 1350 1355 1360

cta aat tat tca ttc aag aac ttt gaa gtg cag aaa tac gaa tgg ctt 4128
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1365 1370 1375

gac caa aaa ttt aac gtg tcg ttg tta ttg gca gaa gta aac gct caa 4176
Asp Gln Lys Phe Asn Val Ser Leu Leu Leu Ala Glu Val Asn Ala Gln
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aag aat ggt aca tta gat ttt tct gtt tta aca aag gtt ttc cgt ctt 4224
Lys Asn Gly Thr Leu Asp Phe Ser Val Leu Thr Lys Val Phe Arg Leu
1395 1400 1405

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1410 1415 1420

gcc gaa gaa att atg gtt gaa gga agt aag att tct gac ttt gtc aca 4320
Ala Glu Glu Ile Met Val Glu Gly Ser Lys Ile Ser Asp Phe Val Thr
1425 1430 1435 1440

aag tac ctg gtg tcg acc gac ttg aag gat gtg cag ttg aaa tgc tta 4368
Lys Tyr Leu Val Ser Thr Asp Leu Lys Asp Val Gln Leu Lys Cys Leu

1445 1450 1455

cat tca tgg tgt caa ttg ata gag att ttg gtt act gac agt gga atc 4416
His Ser Trp Cys Gln Leu Ile Glu Ile Leu Val Thr Asp Ser Gly Ile
1460 1465 1470

aat tcg ctg aat ttc atc ttg gaa gtg ttg caa gtt att att ccc aaa 4464
Asn Ser Leu Asn Phe Ile Leu Glu Val Leu Gln Val Ile Ile Pro Lys
1475 1480 1485

atc aat gac tat ttt gat gtg gac ata ctg ttt tct gaa gaa atg gtt 4512
Ile Asn Asp Tyr Phe Asp Val Asp Ile Leu Phe Ser Glu Glu Met Val
1490 1495 1500

tca tta tgt gtt tta ttg ttt gat ctt tat gat cag ctg act ctt gcg 4560
Ser Leu Cys Val Leu Leu Phe Asp Leu Tyr Asp Gln Leu Thr Leu Ala
1505 1510 1515 1520

gac aga aaa ggt gaa gat ttt gca ctt gga att gag aga ttg atc ccc 4608
Asp Arg Lys Gly Glu Asp Phe Ala Leu Gly Ile Glu Arg Leu Ile Pro
1525 1530 1535

tta ttt cag act tgt att gca ggt att ctt aat tct aac tca aca ccc 4656
Leu Phe Gln Thr Cys Ile Ala Gly Ile Leu Asn Ser Asn Ser Thr Pro
1540 1545 1550

agc tta cgc tca gac ttg tat gta gtt ggc aac aag ttt ttg tta aaa 4704
Ser Leu Arg Ser Asp Leu Tyr Val Val Gly Asn Lys Phe Leu Leu Lys
1555 1560 1565

tgt ttt gag aga gag tcg ttt ttg aaa caa gtg atg cat atc atc aag 4752
Cys Phe Glu Arg Glu Ser Phe Leu Lys Gln Val Met His Ile Ile Lys
1570 1575 1580

tcg gta gat aaa aag ttt ttc cag gtg att tgt aat gac gct atc tac 4800
Ser Val Asp Lys Lys Phe Phe Gln Val Ile Cys Asn Asp Ala Ile Tyr
1585 1590 1595 1600

tca gag ggt cca tct aga atc act tct act tta ttc ctc gag tca tta 4848
Ser Glu Gly Pro Ser Arg Ile Thr Ser Thr Leu Phe Leu Glu Ser Leu
1605 1610 1615

gtt cac tta ggg act ttg gtc aag gtt gat ttt att ttg aat gcg ttg 4896
Val His Leu Gly Thr Leu Val Lys Val Asp Phe Ile Leu Asn Ala Leu
1620 1625 1630

atc aaa aat aac gca ttg ctg ttg cta gtc agg tca gtt aag cgg act 4944
Ile Lys Asn Asn Ala Leu Leu Leu Leu Val Arg Ser Val Lys Arg Thr
1635 1640 1645

gat gcc atg atc aaa ttg tgc cag gaa aaa aat tca gga gtg act tta 4992
Asp Ala Met Ile Lys Leu Cys Gln Glu Lys Asn Ser Gly Val Thr Leu
1650 1655 1660

gat cat ttc ata ttt gac ttg atg gca ttc aaa gca acg cta tat ttt 5040
Asp His Phe Ile Phe Asp Leu Met Ala Phe Lys Ala Thr Leu Tyr Phe
1665 1670 1675 1680

09786880.060101

ttt gtt aga gtg gcc aaa tcg aaa aac ggg gca ttg cag ttg att caa 5088
Phe Val Arg Val Ala Lys Ser Lys Asn Gly Ala Leu Gln Leu Ile Gln
1685 1690 1695

aat gaa ttg ttt tca att ttg cat cag tcg aag ttt ttg cag att gat 5136
Asn Glu Leu Phe Ser Ile Leu His Gln Ser Lys Phe Leu Gln Ile Asp
1700 1705 1710

cca gat att ggt tta agt tta cga att gaa gaa gtt caa gat cac aag 5184
Pro Asp Ile Gly Leu Ser Leu Arg Ile Glu Glu Val Gln Asp His Lys
1715 1720 1725

act gtc aat gta aat gtt ttg cta gat act cca ctt tcg ata act gac 5232
Thr Val Asn Val Asn Val Leu Leu Asp Thr Pro Leu Ser Ile Thr Asp
1730 1735 1740

ttg gtg gat cca tac aag ttg cga agt gaa aac act ata tca tat ttt 5280
Leu Val Asp Pro Tyr Lys Leu Arg Ser Glu Asn Thr Ile Ser Tyr Phe
1745 1750 1755 1760

gag ttc ctt gta cca ata ttt cag cta ctt aca aca gtg tta ttg tca 5328
Glu Phe Leu Val Pro Ile Phe Gln Leu Leu Thr Thr Val Leu Leu Ser
1765 1770 1775

atg gga cca aat tat caa cct gca att att caa act aga gaa ctt atg 5376
Met Gly Pro Asn Tyr Gln Pro Ala Ile Ile Gln Thr Arg Glu Leu Met
1780 1785 1790

aag agt gta aat cga ttg gtg gta ggt gtt atg aaa aga gat ttc ttg 5424
Lys Ser Val Asn Arg Leu Val Val Gly Val Met Lys Arg Asp Phe Leu
1795 1800 1805

gta gag acc aaa caa att ggt caa ggg ttg tac aag gaa gag agt cac 5472
Val Glu Thr Lys Gln Ile Gly Gln Gly Leu Tyr Lys Glu Glu Ser His
1810 1815 1820

gag ttg gta tcg ttg aaa gaa ttg gtg aag ttg ttt att ttg att gat 5520
Glu Leu Val Ser Leu Lys Glu Leu Val Lys Leu Phe Ile Leu Ile Asp
1825 1830 1835 1840

tca tta gct cat tat agt gtg tag 5544
Ser Leu Ala His Tyr Ser Val
1845

<210> 11
<211> 1847
<212> PRT
<213> Candida albicans

<400> 11
Met Ser Gly Ile Phe Asn Trp Ser Leu Asp Val Phe Ala Asp Ile Tyr
1 5 10 15

Asn Thr Leu Lys Phe Glu Ser Asn Ile Asp Leu Asp Thr Ile Asp Phe
20 25 30

Thr Ser Ile Lys Asn Asp Leu Ala Asn Val Leu Ile Thr Pro Val Pro
35 40 45

Leu Asp Gln Ser Arg Ser Lys Leu Gly Asp Ala Ser Lys Pro Val Ala
50 55 60

Leu Pro Ser Gly Asp Glu Val Lys Leu Asn Gln Ala Ser Ile Glu Ile
65 70 75 80

Thr Gly Val Leu Ser Asn Glu Leu Asp Leu Asp Glu Leu Asn Thr Ala
85 90 95

Glu Leu Leu Tyr Asn Ala Ser Asp Leu Ser Tyr Lys Lys Gly Thr Ser
100 105 110

Ile Gly Asp Ser Ala Arg Leu Ala Tyr Tyr Leu Arg Ala His Tyr Ile
115 120 125

Leu Asn Ile Val Gly Tyr Leu Val Ser His Lys Arg Leu Asp Ile Ile
130 135 140

Thr Asn Asn Asn Gln Val Leu Phe Asp Asn Ile Leu Lys Ser Phe Ser
145 150 155 160

Lys Ile Tyr Thr Leu Ser Gly Lys Leu Asn Asp Met Ile Asp Lys Gln
165 170 175

Lys Val Thr Gly Asp Ile Asn Asn Leu Ala Phe Ile Asn Cys Ile Asn
180 185 190

Tyr Ser Arg Ser Gln Leu Phe Asn Ala His Glu Leu Leu Gly Gln Val
195 200 205

Val Phe Gly Leu Ala Asp Asn Tyr Tyr Glu Ser Tyr Gly Thr Leu Asn
210 215 220

Asn Tyr Asn Ser Leu Val Glu Phe Ile Leu Lys Asn Ile Ser Asp Glu
225 230 235 240

Asp Val Phe Val Ile His Phe Leu Pro Ser Thr Leu Gln Leu Phe Lys
245 250 255

Lys Leu Leu Gln Leu Gly Glu Glu Ser Leu Val Asp Gln Phe Tyr Lys
260 265 270

Thr Ile Thr Ser Ser Ile Leu Lys Asp Tyr Glu Ala Asn Asn Phe Ser
275 280 285

Lys Ser Glu Asp Ile Asp Leu Ser Lys Ser Lys Leu Ser Gly Phe Glu
290 295 300

Ile Val Thr Ser Phe Ile Phe Leu Thr Glu Phe Ile Pro Trp Cys Lys
305 310 315 320

Gln Leu Ser Ser Arg Thr Ala Lys Tyr Asp Phe Lys Asp Asp Ile Leu
325 330 335

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Lys Tyr Met Glu Phe Leu Ile Ser Tyr Gly Val Met Glu Arg Leu Leu
            340                 345                 350

Ser Tyr Cys Ser Glu Thr Ser Asn Ala Lys Thr Gln Gln Val Tyr Asp
        355                 360                 365

Trp Ser Asn Met Tyr Asp Phe Arg Ala Leu Leu Gln Lys Asn Phe Pro
    370                 375                 380

Arg Leu Thr Pro Ala Lys Phe His Tyr Pro Gly Asn Gln Glu Leu Leu
385                 390                 395                     400

Asn Ala Val Arg Pro Gly Tyr Glu Asn Ile Ser Lys Leu Ile Asp Ile
                405                 410                 415

Ser Phe Leu Thr Leu Asp Pro Ser Leu Asn Glu Thr Leu Val Ser Pro
            420                 425                 430

Phe Phe Gln Ser Phe Phe Ser Val Phe Ile Ser Asn Ala Ala Val Val
        435                 440                 445

Met Thr Ser Leu Arg Asp Ser Glu Glu Asp Phe Val Leu Ser Ser Leu
    450                 455                 460

Asn Glu Ser Asp Glu Glu Glu Glu Glu Glu Glu Ser Asp Ser Asp Glu
465                 470                 475                     480

Asp Ser Ser Thr Pro Lys Asn Lys Glu Lys Ser Ala Gly Leu Asp Leu
                485                 490                 495

Asp Lys Ile Ala Gln Arg Ala Glu Leu Glu Arg Phe Tyr Leu Ala Phe
            500                 505                 510

Ala Tyr Thr Tyr Asn Asn Arg Pro Glu Leu Cys Ala Leu Phe Trp Gly
        515                 520                 525

Asn Glu Gln Val Thr His Asp Ile Ile Gly Phe Ile Ser Trp Gly Leu
    530                 535                 540

Ala Asn Asn Thr Ser Pro Leu Ile Thr Ala Thr Phe Cys Leu Leu Leu
545                 550                 555                     560

Gly Ser Leu Ala Ser Ala Gly Ala Glu Ala Thr Ser Arg Ile Trp Glu
                565                 570                 575

Ile Leu Val His Asn Asn Asn Asn Ala Ser Thr Arg Lys Asn Asp Phe
            580                 585                 590

Ser Lys Val Ser Val Asp Ser Leu Tyr Asp Ser Leu Lys Tyr Tyr Ile
        595                 600                 605

Asp Ser Leu Asn Glu Ser Phe Glu Gln Asp Leu Asn Ala Gln Leu Met
    610                 615                 620

Leu Asn Gln Lys Lys Gln Asp Phe Leu Phe Ser Thr Thr Thr Ser Lys
625                 630                 635                     640
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Gln Asp Leu Asp Asp Ser Gly Glu Asn Arg Ile Val Ile Glu Leu Ala
                645                 650                 655

Glu Asp Ser Leu Val Leu Ile Ser Gly Phe Ile Gln Leu Leu Ser Ala
            660                 665                 670

Ile Val Lys Asn Leu Asn Thr Lys Asn Glu Arg Ser Lys Glu Ile Lys
        675                 680                 685

Ser Val Val Tyr Thr Arg Phe Ser Pro Ile Ile Lys Gly Phe Leu Lys
    690                 695                 700

Phe Asp Asn Leu Ile Asn Gly Ser Arg Phe Leu Gln Val Asp Ala Ser
705                 710                 715                     720

Ile Gln Ser Thr Asn Asn Pro Lys Phe Ile Asp Leu Pro Asn Val Phe
                725                 730                 735

Val Ser Asp Asp Ser Arg Ile Ile Leu Thr Asn Leu Ile Leu Thr Phe
            740                 745                 750

Leu Gly Asp Phe Val Thr Asn Asp Ser Asp Pro Tyr Ile Arg Tyr Glu
        755                 760                 765

Ile Trp Arg Leu Val Asp Arg Trp Met Tyr Gln Gly Leu His Ser Leu
    770                 775                 780

Pro Glu Asp Lys Lys Asp Asp Ala Phe Arg His Ile Lys Arg Lys Tyr
785                 790                 795                     800

Asn Ser Lys Lys Asn Val Pro Ile Asn Gln Ala Phe Ser Thr Asn Leu
                805                 810                 815

Thr His Leu Ser Gln Ile Gly Asn Phe Thr Val Leu Val Lys Lys Leu
            820                 825                 830

Leu Thr Pro Tyr Ala Asp Ser Asn Glu Ala Phe Thr Lys Tyr Ser Leu
        835                 840                 845

Leu Tyr Pro Cys Asp Leu Gly Leu Gly Tyr Arg Phe Asn Asn Gln Leu
    850                 855                 860

Gly Ile Trp Pro Tyr Ile Glu Phe Leu Met Gln Asn Val Phe Ala Asn
865                 870                 875                     880

Ser Gly Thr Ile Ala Asn Lys Arg Asp Arg Val Asn Leu Gln Leu Asn
                885                 890                 895

Leu Leu Glu Leu Phe Ser Asn Ala Leu Gln Gly Val Asp Trp Lys Phe
            900                 905                 910

Leu Ile Asp Val Ala Pro Lys Ile Ile Arg Asp Leu Lys Asn Phe Asn
        915                 920                 925

Gly Ile Phe Asp Ser Leu Ile Pro Gly Val Gln Leu Asp Phe Glu Val
    930                 935                 940
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Phe Val Lys Leu His His Ser Val Ala Val Ile Asn Tyr Leu Phe Glu
945 950 955 960

Asn Arg Thr Phe Ser Ala Leu Phe Lys Leu Val Asn Ile Gly Val Asp
965 970 975

Ser Val Asn Glu Ser Gly Glu Ser Ala Glu Leu Val Ser His Ala Leu
980 985 990

Gly Leu Ile Asn Ser Leu Leu Arg Val Gln Asn Ser Phe Ile Asn Lys
995 1000 1005

Leu Leu Pro Ile Leu Arg Asn Lys Asp Thr Gln Gln Gln Leu His Arg
1010 1015 1020

Gly Thr Ala Ile Gly Ile Gly Thr Ser Met Ser Leu Ala Leu Ala Thr
025 1030 1035 1040

Pro Arg Thr Ile Phe Asp Cys Ile Tyr Tyr Pro Lys Asn Leu Gly Thr
1045 1050 1055

His Gly Val Ala Asp Phe Tyr Glu Val Ile Leu Phe His Leu Ser Ala
1060 1065 1070

Val Val Gln Phe Ala Leu Tyr Val Ser Cys Glu Asn Thr Ile Ser Asn
1075 1080 1085

Lys Ala Ile Ser Ile Leu Lys Gly Val Ser Gln Ser Lys Phe Phe Val
1090 1095 1100

Thr Arg Val Ser Ser Ser Ala Asp Pro Leu Leu Asn Asn Asp Arg Leu
105 1110 1115 1120

Ile Thr Thr Phe Glu Asn Ile Asp Glu Ser Ile Lys Ile Lys Phe Ala
1125 1130 1135

Phe Ile Asp Lys Phe Glu Glu Leu Glu Asp Ser Leu Asn Met Lys Tyr
1140 1145 1150

Glu Ile Leu Asp Phe Val Leu Gly Asn Leu Asn Gln Phe Asp Gly Lys
1155 1160 1165

Val Ala Thr Thr Ala His Phe Leu Leu Gly Tyr Lys Val Lys Gly Asp
1170 1175 1180

Thr Leu Asp Leu Val Gln Thr Asn Asp Gln Asn Thr Leu Leu Lys Ser
185 1190 1195 1200

Phe Leu Asn Thr Leu Ser Ile Ser Leu Asp Leu Ile Ser Glu Ile Asp
1205 1210 1215

Tyr Asn Asn Gly Asn Asn His Ile Ile Asp Val Gly Pro Ala Lys Leu
1220 1225 1230

Ser Ser Leu Ile Leu Gln Ile Leu Ile Lys Leu Cys Gln Asp Pro Ile
1235 1240 1245

Ser Ser Ser Ile Thr Leu Asn Gln Leu Arg Glu Tyr Glu Glu Leu Phe
1250 1255 1260

Glu Lys Leu Val Asn Cys Gln Pro Lys Leu Asp Leu Asn Thr Val Trp
265 1270 1275 1280

Cys Gly Asn Gln Phe Asp Gly Asp Leu Gln Ile Asp Ala Ser Asn Val
1285 1290 1295

Phe Val Asp Asn Gln Ala Ser Thr Gln Ala Phe Phe Ser Phe Ile Asn
1300 1305 1310

Gln Arg Asn Leu Ile Leu Gln Tyr Leu Ser Leu Glu Phe His Ser Val
1315 1320 1325

Lys Ser Arg Thr Lys Arg Glu Tyr Tyr Ser Lys Val Leu Thr Asn Asp
1330 1335 1340

Lys Glu Phe Val Asn Arg Thr Pro Lys Val Leu Thr Phe Leu Asn Ile
345 1350 1355 1360

Leu Asn Tyr Ser Phe Lys Asn Phe Glu Val Gln Lys Tyr Glu Trp Leu
1365 1370 1375

Asp Gln Lys Phe Asn Val Ser Leu Leu Leu Ala Glu Val Asn Ala Gln
1380 1385 1390

Lys Asn Gly Thr Leu Asp Phe Ser Val Leu Thr Lys Val Phe Arg Leu
1395 1400 1405

Leu Cys Gln Thr Ser Asn Leu Ile Thr Pro Glu Ser Lys Gln Leu Phe
1410 1415 1420

Ala Glu Glu Ile Met Val Glu Gly Ser Lys Ile Ser Asp Phe Val Thr
425 1430 1435 1440

Lys Tyr Leu Val Ser Thr Asp Leu Lys Asp Val Gln Leu Lys Cys Leu
1445 1450 1455

His Ser Trp Cys Gln Leu Ile Glu Ile Leu Val Thr Asp Ser Gly Ile
1460 1465 1470

Asn Ser Leu Asn Phe Ile Leu Glu Val Leu Gln Val Ile Ile Pro Lys
1475 1480 1485

Ile Asn Asp Tyr Phe Asp Val Asp Ile Leu Phe Ser Glu Glu Met Val
1490 1495 1500

Ser Leu Cys Val Leu Leu Phe Asp Leu Tyr Asp Gln Leu Thr Leu Ala
505 1510 1515 1520

Asp Arg Lys Gly Glu Asp Phe Ala Leu Gly Ile Glu Arg Leu Ile Pro
1525 1530 1535

Leu Phe Gln Thr Cys Ile Ala Gly Ile Leu Asn Ser Asn Ser Thr Pro
1540 1545 1550

Ser Leu Arg Ser Asp Leu Tyr Val Val Gly Asn Lys Phe Leu Leu Lys
1555 1560 1565

Cys Phe Glu Arg Glu Ser Phe Leu Lys Gln Val Met His Ile Ile Lys
1570 1575 1580

Ser Val Asp Lys Lys Phe Phe Gln Val Ile Cys Asn Asp Ala Ile Tyr
585 1590 1595 1600

Ser Glu Gly Pro Ser Arg Ile Thr Ser Thr Leu Phe Leu Glu Ser Leu
1605 1610 1615

Val His Leu Gly Thr Leu Val Lys Val Asp Phe Ile Leu Asn Ala Leu
1620 1625 1630

Ile Lys Asn Asn Ala Leu Leu Leu Leu Val Arg Ser Val Lys Arg Thr
1635 1640 1645

Asp Ala Met Ile Lys Leu Cys Gln Glu Lys Asn Ser Gly Val Thr Leu
1650 1655 1660

Asp His Phe Ile Phe Asp Leu Met Ala Phe Lys Ala Thr Leu Tyr Phe
665 1670 1675 1680

Phe Val Arg Val Ala Lys Ser Lys Asn Gly Ala Leu Gln Leu Ile Gln
1685 1690 1695

Asn Glu Leu Phe Ser Ile Leu His Gln Ser Lys Phe Leu Gln Ile Asp
1700 1705 1710

Pro Asp Ile Gly Leu Ser Leu Arg Ile Glu Glu Val Gln Asp His Lys
1715 1720 1725

Thr Val Asn Val Asn Val Leu Leu Asp Thr Pro Leu Ser Ile Thr Asp
1730 1735 1740

Leu Val Asp Pro Tyr Lys Leu Arg Ser Glu Asn Thr Ile Ser Tyr Phe
745 1750 1755 1760

Glu Phe Leu Val Pro Ile Phe Gln Leu Leu Thr Thr Val Leu Leu Ser
1765 1770 1775

Met Gly Pro Asn Tyr Gln Pro Ala Ile Ile Gln Thr Arg Glu Leu Met
1780 1785 1790

Lys Ser Val Asn Arg Leu Val Val Gly Val Met Lys Arg Asp Phe Leu
1795 1800 1805

Val Glu Thr Lys Gln Ile Gly Gln Gly Leu Tyr Lys Glu Glu Ser His
1810 1815 1820

Glu Leu Val Ser Leu Lys Glu Leu Val Lys Leu Phe Ile Leu Ile Asp
825 1830 1835 1840

Ser Leu Ala His Tyr Ser Val
1845

<210> 12
<211> 575
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Probe

<400> 12
gtttggtgac tcaacctacc accaatcgat ttacactctt cataagttct ctagtttgaa 60

taattgcagg ttgataattt ggtcccattg acaataacac tgttgtaagt agctgaaata 120

ttggtacaag gaactcaaaa tatgatatag tgttttcact tcgcaacttg tatggatcca 180

ccaagtcagt tatcgaaagt ggagtatcta gcaaaacatt tacattgaca gtcttgtgat 240

cttgaacttc ttcaattcgt aaacttaaac caatatctgg atcaatctgc aaaaacttcg 300

actgatgcaa aattgaaaac aattcatttt ggaatcannn nnanaantna aaaaaaatat 360

atattntntt tttttttttt ttntttnttt tttattttat cttacannac accccaacac 420

aacacccaac ccnaaaacac ccaacacctc catcttgtcc cgcttttctc tcacattttt 480

tctctactac tatcacacaa tctataaaac atacaccccc tcaacccctc ctccccaaca 540

aacctacctc cctcaactcc tatttcctcc cttcc 575

<210> 13
<211> 921
<212> DNA
<213> Candida albicans

<220>
<221> CDS
<222> (1)..(918)

<220>
<221> gene
<222> (1)..(918)
<223> gene CaOR110

<400> 13
atg acg att gaa act att tat atc gca aga cac ggt tat aga tcc aat 48
Met Thr Ile Glu Thr Ile Tyr Ile Ala Arg His Gly Tyr Arg Ser Asn
1 5 10 15

tgg tta cca cca cca cac cca cca aat cct act ggt att gac agt gac 96
Trp Leu Pro Pro Pro His Pro Pro Asn Pro Thr Gly Ile Asp Ser Asp
20 25 30

ccg gct tta gca cca cat ggt gtt gaa caa gcc caa cag tta gct gcc 144
Pro Ala Leu Ala Pro His Gly Val Glu Gln Ala Gln Gln Leu Ala Ala

35 40 45

tat ctt aca tca tta cct aca cat gaa aag cct gaa ttt att att gct 192
Tyr Leu Thr Ser Leu Pro Thr His Glu Lys Pro Glu Phe Ile Ile Ala
50 55 60

tca cct ttt tat cgt tgt ata gaa acg tcg aga ccc att gcc gaa atg 240
Ser Pro Phe Tyr Arg Cys Ile Glu Thr Ser Arg Pro Ile Ala Glu Met
65 70 75 80

ttg gac ttg aag att gct tta gaa aga gga gtt ggt gaa tgg ttt cgt 288
Leu Asp Leu Lys Ile Ala Leu Glu Arg Gly Val Gly Glu Trp Phe Arg
85 90 95

aaa aat aga gat acc aaa cca gtt ccc ggt gat tac aca caa ttg aga 336
Lys Asn Arg Asp Thr Lys Pro Val Pro Gly Asp Tyr Thr Gln Leu Arg
100 105 110

aca ttt ttc gat aaa tta ttg atc gat gaa gat act tgg cca aga gat 384
Thr Phe Phe Asp Lys Leu Leu Ile Asp Glu Asp Thr Trp Pro Arg Asp
115 120 125

aac tta aat gtt ata cct aat att gaa gga gaa gat tat gat gaa atc 432
Asn Leu Asn Val Ile Pro Asn Ile Glu Gly Glu Asp Tyr Asp Glu Ile
130 135 140

tac gat cgt gcc aaa ttg ttt tgg aaa aag ttt att cct gaa ttt gaa 480
Tyr Asp Arg Ala Lys Leu Phe Trp Lys Lys Phe Ile Pro Glu Phe Glu
145 150 155 160

aag aaa ttc ccc gaa att aaa aat gtg ttg ata gtt aca cat gca gca 528
Lys Lys Phe Pro Glu Ile Lys Asn Val Leu Ile Val Thr His Ala Ala
165 170 175

acg aaa att gct tta gga tca gct tta tta cag tta aaa tca gtt act 576
Thr Lys Ile Ala Leu Gly Ser Ala Leu Leu Gln Leu Lys Ser Val Thr
180 185 190

gat gtt ata gat gat aat caa act gtg tta cgt gct ggt gca tgt tca 624
Asp Val Ile Asp Asp Asn Gln Thr Val Leu Arg Ala Gly Ala Cys Ser
195 200 205

tta tcc aaa ttt gtt aga gat ggc gaa gat aaa acc aat cat act att 672
Leu Ser Lys Phe Val Arg Asp Gly Glu Asp Lys Thr Asn His Thr Ile
210 215 220

caa tgg aaa att gtc atg aat ggt aat tgt gaa ttc ttg aca cag ggt 720
Gln Trp Lys Ile Val Met Asn Gly Asn Cys Glu Phe Leu Thr Gln Gly
225 230 235 240

gaa gaa atg aac tgg gat ttc cgt cgt ggt gtt gaa gcc ggg tca gct 768
Glu Glu Met Asn Trp Asp Phe Arg Arg Gly Val Glu Ala Gly Ser Ala
245 250 255

gaa gat ata gcg caa aga aag gca gca gca gaa gca gaa gca aaa gca 816
Glu Asp Ile Ala Gln Arg Lys Ala Ala Ala Glu Ala Glu Ala Lys Ala
260 265 270

ttg aag aaa aat gaa caa acc aaa tcc gat ggt ccc atc act gaa tct 864
Leu Lys Lys Asn Glu Gln Thr Lys Ser Asp Gly Pro Ile Thr Glu Ser
275 280 285

gcc act ggg gca gaa ata gat ggg aat gaa gat gaa ttt gaa gta cgt 912
Ala Thr Gly Ala Glu Ile Asp Gly Asn Glu Asp Glu Phe Glu Val Arg
290 295 300

aaa act tga 921
Lys Thr
305

<210> 14
<211> 306
<212> PRT
<213> Candida albicans

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Met Thr Ile Glu Thr Ile Tyr Ile Ala Arg His Gly Tyr Arg Ser Asn
1 5 10 15

Trp Leu Pro Pro Pro His Pro Pro Asn Pro Thr Gly Ile Asp Ser Asp
20 25 30

Pro Ala Leu Ala Pro His Gly Val Glu Gln Ala Gln Gln Leu Ala Ala
35 40 45

Tyr Leu Thr Ser Leu Pro Thr His Glu Lys Pro Glu Phe Ile Ile Ala
50 55 60

Ser Pro Phe Tyr Arg Cys Ile Glu Thr Ser Arg Pro Ile Ala Glu Met
65 70 75 80

Leu Asp Leu Lys Ile Ala Leu Glu Arg Gly Val Gly Glu Trp Phe Arg
85 90 95

Lys Asn Arg Asp Thr Lys Pro Val Pro Gly Asp Tyr Thr Gln Leu Arg
100 105 110

Thr Phe Phe Asp Lys Leu Leu Ile Asp Glu Asp Thr Trp Pro Arg Asp
115 120 125

Asn Leu Asn Val Ile Pro Asn Ile Glu Gly Glu Asp Tyr Asp Glu Ile
130 135 140

Tyr Asp Arg Ala Lys Leu Phe Trp Lys Lys Phe Ile Pro Glu Phe Glu
145 150 155 160

Lys Lys Phe Pro Glu Ile Lys Asn Val Leu Ile Val Thr His Ala Ala
165 170 175

Thr Lys Ile Ala Leu Gly Ser Ala Leu Leu Gln Leu Lys Ser Val Thr
180 185 190

Asp Val Ile Asp Asp Asn Gln Thr Val Leu Arg Ala Gly Ala Cys Ser

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        195                 200                 205

Leu Ser Lys Phe Val Arg Asp Gly Glu Asp Lys Thr Asn His Thr Ile
    210                 215                 220

Gln Trp Lys Ile Val Met Asn Gly Asn Cys Glu Phe Leu Thr Gln Gly
225                 230                 235                     240

Glu Glu Met Asn Trp Asp Phe Arg Arg Gly Val Glu Ala Gly Ser Ala
                245                 250                 255

Glu Asp Ile Ala Gln Arg Lys Ala Ala Ala Glu Ala Glu Ala Lys Ala
            260                 265                 270

Leu Lys Lys Asn Glu Gln Thr Lys Ser Asp Gly Pro Ile Thr Glu Ser
        275                 280                 285

Ala Thr Gly Ala Glu Ile Asp Gly Asn Glu Asp Glu Phe Glu Val Arg
    290                 295                 300

Lys Thr
305


<210> 15
<211> 1454
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Splice Variant

<220>
<221> CDS
<222> (1)..(1452)
<223> gene CaOR110 Splice Variant

<400> 15
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Met Thr Ile Glu Thr Ile Tyr Ile Ala Arg His Gly Tyr Arg Ser Asn
  1               5                  10                  15

tgg tta cca cca cca cac cca cca aat cct act ggt att gac agt gac      96
Trp Leu Pro Pro Pro His Pro Pro Asn Pro Thr Gly Ile Asp Ser Asp
             20                  25                  30

ccg gct tta gca cca cat ggt gtt gaa caa gcc caa cag tta gct gcc     144
Pro Ala Leu Ala Pro His Gly Val Glu Gln Ala Gln Gln Leu Ala Ala
         35                  40                  45

tat ctt aca tca tta cct aca cat gaa aag cct gaa ttt att att gct     192
Tyr Leu Thr Ser Leu Pro Thr His Glu Lys Pro Glu Phe Ile Ile Ala
     50                  55                  60

tca cct ttt tat cgt tgt ata gaa acg tcg aga ccc att gcc gaa atg     240
Ser Pro Phe Tyr Arg Cys Ile Glu Thr Ser Arg Pro Ile Ala Glu Met
 65                  70                  75                  80
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ttg gac ttg aag att gct tta gaa aga gga gtt ggt gaa tgg ttt cgt    288
Leu Asp Leu Lys Ile Ala Leu Glu Arg Gly Val Gly Glu Trp Phe Arg
                 85                  90                  95

aaa aat aga gat acc aaa cca gtt ccc ggt gat tac aca caa ttg aga    336
Lys Asn Arg Asp Thr Lys Pro Val Pro Gly Asp Tyr Thr Gln Leu Arg
            100                 105                 110

aca ttt ttc gat aaa tta ttg atc gat gaa gat act tgg cca aga gat    384
Thr Phe Phe Asp Lys Leu Leu Ile Asp Glu Asp Thr Trp Pro Arg Asp
        115                 120                 125

aac tta aat gtt ata cct aat att gaa gga gaa gat tat gat gaa atc    432
Asn Leu Asn Val Ile Pro Asn Ile Glu Gly Glu Asp Tyr Asp Glu Ile
    130                 135                 140

tac gat cgt gcc aaa ttg ttt tgg aaa aag ttt att cct gaa ttt gaa    480
Tyr Asp Arg Ala Lys Leu Phe Trp Lys Lys Phe Ile Pro Glu Phe Glu
145                 150                 155                 160

aag aaa ttc ccc gaa att aaa aat gtg ttg ata gtt aca cat gca gca    528
Lys Lys Phe Pro Glu Ile Lys Asn Val Leu Ile Val Thr His Ala Ala
                165                 170                 175

acg aaa att gct tta gga tca gct tta tta cag tta aaa tca gtt act    576
Thr Lys Ile Ala Leu Gly Ser Ala Leu Leu Gln Leu Lys Ser Val Thr
            180                 185                 190

gat gtt ata gat gat aat caa act gtg tta cgt gct ggt gca tgt tca    624
Asp Val Ile Asp Asp Asn Gln Thr Val Leu Arg Ala Gly Ala Cys Ser
        195                 200                 205

tta tcc aaa ttt gtt aga gat ggc gaa gat aaa acc aat cat act att    672
Leu Ser Lys Phe Val Arg Asp Gly Glu Asp Lys Thr Asn His Thr Ile
    210                 215                 220

caa tgg aaa att gtc atg aat ggt aat tgt gaa ttc ttg aca cag ggt    720
Gln Trp Lys Ile Val Met Asn Gly Asn Cys Glu Phe Leu Thr Gln Gly
225                 230                 235                 240

gaa gaa atg aac tgg gat ttc cgt cgt ggt gtt gaa gcc ggg tca gct    768
Glu Glu Met Asn Trp Asp Phe Arg Arg Gly Val Glu Ala Gly Ser Ala
                245                 250                 255

gaa gat ata gcg caa aga aag gca gca gca gaa gca gaa gca aaa gca    816
Glu Asp Ile Ala Gln Arg Lys Ala Ala Ala Glu Ala Glu Ala Lys Ala
            260                 265                 270

ttg aag aaa aat gaa caa acc aaa tcc gat ggt ccc atc act gaa tct    864
Leu Lys Lys Asn Glu Gln Thr Lys Ser Asp Gly Pro Ile Thr Glu Ser
        275                 280                 285

gcc act ggg gca gaa ata gat ggg aat gaa gat gaa ttt gaa aca ttt    912
Ala Thr Gly Ala Glu Ile Asp Gly Asn Glu Asp Glu Phe Glu Thr Phe
    290                 295                 300
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tat gta acc atc gat ata cct tca att tcg aat aaa atc gac aat gaa 960
Tyr Val Thr Ile Asp Ile Pro Ser Ile Ser Asn Lys Ile Asp Asn Glu
305 310 315 320

gaa gaa cca cca tca agg aca ggt caa gct cca aaa ttc aaa aac aat 1008
Glu Glu Pro Pro Ser Arg Thr Gly Gln Ala Pro Lys Phe Lys Asn Asn
325 330 335

att atc aag cct tca gca caa ctc caa ttt act gat tta aaa gaa gat 1056
Ile Ile Lys Pro Ser Ala Gln Leu Gln Phe Thr Asp Leu Lys Glu Asp
340 345 350

cat cca tta gta aaa ata tcg aac aat act ata tct gct caa ggc tcg 1104
His Pro Leu Val Lys Ile Ser Asn Asn Thr Ile Ser Ala Gln Gly Ser
355 360 365

tcg tcg tcg tcg tta tca gcg tcg aaa aat gga ttt aat agt cat act 1152
Ser Ser Ser Ser Leu Ser Ala Ser Lys Asn Gly Phe Asn Ser His Thr
370 375 380

cac aat tca gga gtc att gat cca tca gca ctt ata gat ggg aaa att 1200
His Asn Ser Gly Val Ile Asp Pro Ser Ala Leu Ile Asp Gly Lys Ile
385 390 395 400

tat cag act gat tgg aat caa tta caa ggt act gaa cta ata ttt gat 1248
Tyr Gln Thr Asp Trp Asn Gln Leu Gln Gly Thr Glu Leu Ile Phe Asp
405 410 415

gaa aat ggt caa ttt ata ggc aag gtt aag gaa cat ttg act tgc aat 1296
Glu Asn Gly Gln Phe Ile Gly Lys Val Lys Glu His Leu Thr Cys Asn
420 425 430

aat aac aca aaa ttc aca tta aaa aag gca gaa gaa gta gaa caa ctt 1344
Asn Asn Thr Lys Phe Thr Leu Lys Lys Ala Glu Glu Val Glu Gln Leu
435 440 445

cgt tca gca gat gat tct atc atg gat ata gat caa gac tca caa gga 1392
Arg Ser Ala Asp Asp Ser Ile Met Asp Ile Asp Gln Asp Ser Gln Gly
450 455 460

caa caa cca gct aga agt cag ttc tta aaa aga gca att gtg gct gct 1440
Gln Gln Pro Ala Arg Ser Gln Phe Leu Lys Arg Ala Ile Val Ala Ala
465 470 475 480

aga gcc aaa ggt aa 1454
Arg Ala Lys Gly

<210> 16
<211> 484
<212> PRT
<213> Artificial Sequence
<223> Description of Artificial Sequence: Splice Variant

<400> 16
Met Thr Ile Glu Thr Ile Tyr Ile Ala Arg His Gly Tyr Arg Ser Asn
1 5 10 15

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Trp Leu Pro Pro Pro His Pro Pro Asn Pro Thr Gly Ile Asp Ser Asp
            20                  25                  30

Pro Ala Leu Ala Pro His Gly Val Glu Gln Ala Gln Gln Leu Ala Ala
        35                  40                  45

Tyr Leu Thr Ser Leu Pro Thr His Glu Lys Pro Glu Phe Ile Ile Ala
    50                  55                  60

Ser Pro Phe Tyr Arg Cys Ile Glu Thr Ser Arg Pro Ile Ala Glu Met
65                  70                  75                      80

Leu Asp Leu Lys Ile Ala Leu Glu Arg Gly Val Gly Glu Trp Phe Arg
                85                  90                  95

Lys Asn Arg Asp Thr Lys Pro Val Pro Gly Asp Tyr Thr Gln Leu Arg
            100                 105                 110

Thr Phe Phe Asp Lys Leu Leu Ile Asp Glu Asp Thr Trp Pro Arg Asp
        115                 120                 125

Asn Leu Asn Val Ile Pro Asn Ile Glu Gly Glu Asp Tyr Asp Glu Ile
    130                 135                 140

Tyr Asp Arg Ala Lys Leu Phe Trp Lys Lys Phe Ile Pro Glu Phe Glu
145                 150                 155                     160

Lys Lys Phe Pro Glu Ile Lys Asn Val Leu Ile Val Thr His Ala Ala
                165                 170                 175

Thr Lys Ile Ala Leu Gly Ser Ala Leu Leu Gln Leu Lys Ser Val Thr
            180                 185                 190

Asp Val Ile Asp Asp Asn Gln Thr Val Leu Arg Ala Gly Ala Cys Ser
        195                 200                 205

Leu Ser Lys Phe Val Arg Asp Gly Glu Asp Lys Thr Asn His Thr Ile
    210                 215                 220

Gln Trp Lys Ile Val Met Asn Gly Asn Cys Glu Phe Leu Thr Gln Gly
225                 230                 235                     240

Glu Glu Met Asn Trp Asp Phe Arg Arg Gly Val Glu Ala Gly Ser Ala
                245                 250                 255

Glu Asp Ile Ala Gln Arg Lys Ala Ala Ala Glu Ala Glu Ala Lys Ala
            260                 265                 270

Leu Lys Lys Asn Glu Gln Thr Lys Ser Asp Gly Pro Ile Thr Glu Ser
        275                 280                 285

Ala Thr Gly Ala Glu Ile Asp Gly Asn Glu Asp Glu Phe Glu Thr Phe
    290                 295                 300

Tyr Val Thr Ile Asp Ile Pro Ser Ile Ser Asn Lys Ile Asp Asn Glu
305                 310                 315                     320
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Glu Glu Pro Pro Ser Arg Thr Gly Gln Ala Pro Lys Phe Lys Asn Asn
                325                 330                 335

Ile Ile Lys Pro Ser Ala Gln Leu Gln Phe Thr Asp Leu Lys Glu Asp
            340                 345                 350

His Pro Leu Val Lys Ile Ser Asn Asn Thr Ile Ser Ala Gln Gly Ser
        355                 360                 365

Ser Ser Ser Ser Leu Ser Ala Ser Lys Asn Gly Phe Asn Ser His Thr
    370                 375                 380

His Asn Ser Gly Val Ile Asp Pro Ser Ala Leu Ile Asp Gly Lys Ile
385                 390                 395                 400

Tyr Gln Thr Asp Trp Asn Gln Leu Gln Gly Thr Glu Leu Ile Phe Asp
                405                 410                 415

Glu Asn Gly Gln Phe Ile Gly Lys Val Lys Glu His Leu Thr Cys Asn
            420                 425                 430

Asn Asn Thr Lys Phe Thr Leu Lys Lys Ala Glu Glu Val Glu Gln Leu
        435                 440                 445

Arg Ser Ala Asp Asp Ser Ile Met Asp Ile Asp Gln Asp Ser Gln Gly
    450                 455                 460

Gln Gln Pro Ala Arg Ser Gln Phe Leu Lys Arg Ala Ile Val Ala Ala
465                 470                 475                 480

Arg Ala Lys Gly


<210> 17
<211> 2877
<212> DNA
<213> Candida albicans

<220>
<221> CDS
<222> (1)..(2874)

<220>
<221> gene
<222> (1)..(2874)
<223> gene CaMR212

<400> 17
atg aat ttg ttt caa cat aaa cat caa aaa tta ata tta caa tgt tat      48
Met Asn Leu Phe Gln His Lys His Gln Lys Leu Ile Leu Gln Cys Tyr
  1               5                  10                  15

cct gct ggg aaa gca gtg gac aaa aaa ccc aac tcg tcc gag tta agt      96
Pro Ala Gly Lys Ala Val Asp Lys Lys Pro Asn Ser Ser Glu Leu Ser
             20                  25                  30
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tat tta tta tac tat gca tcc act cgt aga gtc aaa tta gaa aag gtg     144
Tyr Leu Leu Tyr Tyr Ala Ser Thr Arg Arg Val Lys Leu Glu Lys Val
         35                  40                  45

att aat ttt ttg aaa gat aaa act cat cat gat gtt ggt aga aac cgt     192
Ile Asn Phe Leu Lys Asp Lys Thr His His Asp Val Gly Arg Asn Arg
     50                  55                  60

act ggt aat tta caa gtc aca tta gcc att att cag gaa tta atc aaa     240
Thr Gly Asn Leu Gln Val Thr Leu Ala Ile Ile Gln Glu Leu Ile Lys
 65                  70                  75                  80

aaa tgt agt gaa aac ttg aat gtt ttt gcc ttt caa gtg tgc tat atc     288
Lys Cys Ser Glu Asn Leu Asn Val Phe Ala Phe Gln Val Cys Tyr Ile
                 85                  90                  95

ttg caa ctg att gcc aac act aag gat ctt gcc ttg tgt aaa aat gtt     336
Leu Gln Leu Ile Ala Asn Thr Lys Asp Leu Ala Leu Cys Lys Asn Val
            100                 105                 110

gtc aaa aca ttt ggt gtt ttg tgt gaa aac ttg gat ggt ggg ttg ttc     384
Val Lys Thr Phe Gly Val Leu Cys Glu Asn Leu Asp Gly Gly Leu Phe
        115                 120                 125

aca ggt gat aag gag ttt ata aag att ttc act gaa gtt ttc caa aca     432
Thr Gly Asp Lys Glu Phe Ile Lys Ile Phe Thr Glu Val Phe Gln Thr
    130                 135                 140

tta gtt tcc ttt ggt aag gac aga tcg ggt gtt act cag tat gat tgg     480
Leu Val Ser Phe Gly Lys Asp Arg Ser Gly Val Thr Gln Tyr Asp Trp
145                 150                 155                 160

cag atg att tct tta atg gct ata aat gat ata tcc agt tgt ttg agt     528
Gln Met Ile Ser Leu Met Ala Ile Asn Asp Ile Ser Ser Cys Leu Ser
                165                 170                 175

tat aat gca gct gtt ggt aaa aag ttt att gct ttg tcg att cct gtt     576
Tyr Asn Ala Ala Val Gly Lys Lys Phe Ile Ala Leu Ser Ile Pro Val
            180                 185                 190

tta ctt cag ttt att att gca aac aac cca caa agc agc ata ttg caa     624
Leu Leu Gln Phe Ile Ile Ala Asn Asn Pro Gln Ser Ser Ile Leu Gln
        195                 200                 205

aga ttg aaa tcg aat ctc cac gtt gaa gat gat ggg aag agg ttg tca     672
Arg Leu Lys Ser Asn Leu His Val Glu Asp Asp Gly Lys Arg Leu Ser
    210                 215                 220

cgt gct cat ctg caa aaa tcc cat agc aaa att gcc caa caa att gat     720
Arg Ala His Leu Gln Lys Ser His Ser Lys Ile Ala Gln Gln Ile Asp
225                 230                 235                 240

gat gat ttc acc aat gat tct tta acc ttg aca gat atc act gaa aag     768
Asp Asp Phe Thr Asn Asp Ser Leu Thr Leu Thr Asp Ile Thr Glu Lys
                245                 250                 255

gca ttt tcg tcg atg aaa tct ttt ttc aat acc aat gct gcc agt caa     816
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Ala Phe Ser Ser Met Lys Ser Phe Phe Asn Thr Asn Ala Ala Ser Gln
            260                 265                 270

atc tct gaa gtg aca aga gct gtt gtc caa cac aat att ctc aat gga      864
Ile Ser Glu Val Thr Arg Ala Val Val Gln His Asn Ile Leu Asn Gly
        275                 280                 285

acc gat ttg gag tgg gga gtc tca ttc ttg gaa tta tgt att act tgg      912
Thr Asp Leu Glu Trp Gly Val Ser Phe Leu Glu Leu Cys Ile Thr Trp
    290                 295                 300

att cca gtt caa tta cgt ttt gtc agt ttg tcc acc ttg ttg gcc act      960
Ile Pro Val Gln Leu Arg Phe Val Ser Leu Ser Thr Leu Leu Ala Thr
305                 310                 315                 320

tta ggt aga att aat att gaa ggt aac acc aaa tcc aat tac aac atg      1008
Leu Gly Arg Ile Asn Ile Glu Gly Asn Thr Lys Ser Asn Tyr Asn Met
                325                 330                 335

caa ttc cag tat gct cgt tac ttg tta gga tta ctt tca tct cgt gtg      1056
Gln Phe Gln Tyr Ala Arg Tyr Leu Leu Gly Leu Leu Ser Ser Arg Val
            340                 345                 350

aac atg att ggg tta tca gtt tca gat att att caa cag ttg tta tcg      1104
Asn Met Ile Gly Leu Ser Val Ser Asp Ile Ile Gln Gln Leu Leu Ser
        355                 360                 365

ttg caa gct gat ttg att ttg aag gca agt gat ttg gac aaa agt gaa      1152
Leu Gln Ala Asp Leu Ile Leu Lys Ala Ser Asp Leu Asp Lys Ser Glu
    370                 375                 380

att tca att tta aca gac att tat tct gac tgt att tgt agt ttg act      1200
Ile Ser Ile Leu Thr Asp Ile Tyr Ser Asp Cys Ile Cys Ser Leu Thr
385                 390                 395                 400

aca cat ata tat tac ttt gat caa gtc ccg gac tcg att caa gaa atc      1248
Thr His Ile Tyr Tyr Phe Asp Gln Val Pro Asp Ser Ile Gln Glu Ile
                405                 410                 415

tta atc aag att gat tac att tta gaa agc agt ttt gtg gaa gat aat      1296
Leu Ile Lys Ile Asp Tyr Ile Leu Glu Ser Ser Phe Val Glu Asp Asn
            420                 425                 430

aac att acg tcc act gga gaa caa att caa gat ttg att atc caa ttg      1344
Asn Ile Thr Ser Thr Gly Glu Gln Ile Gln Asp Leu Ile Ile Gln Leu
        435                 440                 445

ttg gat aac att tcg aag att ttt tta att ttg aag aat aaa tca agc      1392
Leu Asp Asn Ile Ser Lys Ile Phe Leu Ile Leu Lys Asn Lys Ser Ser
    450                 455                 460

tca att aat cgt aac cat gtg aat ttg gaa cat tgg gat atc agt tta      1440
Ser Ile Asn Arg Asn His Val Asn Leu Glu His Trp Asp Ile Ser Leu
465                 470                 475                 480

gga tta ttg gct cca caa ggc gac cat gat gat aac aga aaa atg att      1488
Gly Leu Leu Ala Pro Gln Gly Asp His Asp Asp Asn Arg Lys Met Ile
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485 490 495

att tct acg aca caa ctt atc aat atc caa gcc agg tac ttg aaa gtg 1536
Ile Ser Thr Thr Gln Leu Ile Asn Ile Gln Ala Arg Tyr Leu Lys Val
500 505 510

ttt gat gag ttt ttg aat aat gaa ttg gcg gtt ggc aat tct aaa aag 1584
Phe Asp Glu Phe Leu Asn Asn Glu Leu Ala Val Gly Asn Ser Lys Lys
515 520 525

agc tat gat ctt ctt agc aaa cag tct cgt ttg gat cct gga agt aca 1632
Ser Tyr Asp Leu Leu Ser Lys Gln Ser Arg Leu Asp Pro Gly Ser Thr
530 535 540

gct gtt gaa gga gtg aac aag tct gac gat ctg gac aat ggt aag gac 1680
Ala Val Glu Gly Val Asn Lys Ser Asp Asp Leu Asp Asn Gly Lys Asp
545 550 555 560

ttt aaa aaa cct gat gcc aat caa tac att acc aat caa caa aac ttc 1728
Phe Lys Lys Pro Asp Ala Asn Gln Tyr Ile Thr Asn Gln Gln Asn Phe
565 570 575

ata tcc cat ttc ctt atg tat atc gac aaa ttt ttc gaa aat tac gat 1776
Ile Ser His Phe Leu Met Tyr Ile Asp Lys Phe Phe Glu Asn Tyr Asp
580 585 590

tcc ccc aac aca caa tca gtg tta ctt ttg gtt act gtt tta aaa gat 1824
Ser Pro Asn Thr Gln Ser Val Leu Leu Leu Val Thr Val Leu Lys Asp
595 600 605

atg atg aac att tta gga ttg aat ttc ttg agt aat ttt att cca ttt 1872
Met Met Asn Ile Leu Gly Leu Asn Phe Leu Ser Asn Phe Ile Pro Phe
610 615 620

ttc cac cat tgg gtt atg aaa gta aac aga gcc agt aat ttc act caa 1920
Phe His His Trp Val Met Lys Val Asn Arg Ala Ser Asn Phe Thr Gln
625 630 635 640

aga cag aaa ttc aaa gat act ttt gct cat att att tta tat tac atg 1968
Arg Gln Lys Phe Lys Asp Thr Phe Ala His Ile Ile Leu Tyr Tyr Met
645 650 655

ttg aaa gat ttg gat gag caa tat agt cat gat tta caa aat tat tgc 2016
Leu Lys Asp Leu Asp Glu Gln Tyr Ser His Asp Leu Gln Asn Tyr Cys
660 665 670

aaa agc tct aaa tta ttc aaa caa ata ttg gat gct gtt gaa tat aga 2064
Lys Ser Ser Lys Leu Phe Lys Gln Ile Leu Asp Ala Val Glu Tyr Arg
675 680 685

aaa atg caa aag ttt tgg gtc cat ggc att gac cct tca cca tct gat 2112
Lys Met Gln Lys Phe Trp Val His Gly Ile Asp Pro Ser Pro Ser Asp
690 695 700

ttg gaa aac act aaa ggc gac cgt acg ata ccc aca gat gcc aat ggt 2160
Leu Glu Asn Thr Lys Gly Asp Arg Thr Ile Pro Thr Asp Ala Asn Gly
705 710 715 720

aat tat att gct att aga atc aaa cct gaa aat att gag gaa ttt gcc 2208
Asn Tyr Ile Ala Ile Arg Ile Lys Pro Glu Asn Ile Glu Glu Phe Ala
725 730 735

tgt ggt aac aac ttt ttg att gta tgg tta cat ccc caa aaa caa tta 2256
Cys Gly Asn Asn Phe Leu Ile Val Trp Leu His Pro Gln Lys Gln Leu
740 745 750

ctc act gaa att gaa aaa tca caa gtc agt act cat atg agc aca ttc 2304
Leu Thr Glu Ile Glu Lys Ser Gln Val Ser Thr His Met Ser Thr Phe
755 760 765

aat aat gat tct aga aac aca aat atg aca gtg ata atg gat caa gga 2352
Asn Asn Asp Ser Arg Asn Thr Asn Met Thr Val Ile Met Asp Gln Gly
770 775 780

tca ctg gca cta agt gga ggt gca gac cat gga ggt cac ttt gtt ccg 2400
Ser Leu Ala Leu Ser Gly Gly Ala Asp His Gly Gly His Phe Val Pro
785 790 795 800

cca cct gaa ttt gtt aac cac acc ggt ttg tct tct gaa tct gcg tca 2448
Pro Pro Glu Phe Val Asn His Thr Gly Leu Ser Ser Glu Ser Ala Ser
805 810 815

tca aac tca gag aaa ggt ttg tat act ggt tta gga ttg ggt act gct 2496
Ser Asn Ser Glu Lys Gly Leu Tyr Thr Gly Leu Gly Leu Gly Thr Ala
820 825 830

ggt gat att act atg att cat tct gaa ata tta caa tac agt caa cat 2544
Gly Asp Ile Thr Met Ile His Ser Glu Ile Leu Gln Tyr Ser Gln His
835 840 845

ttc caa gaa aga ggt tta cct cat ggt aat ggg ttt gct act att tta 2592
Phe Gln Glu Arg Gly Leu Pro His Gly Asn Gly Phe Ala Thr Ile Leu
850 855 860

cga act gtc gat agt gtt aac agt act aat gat ggg tta att tat act 2640
Arg Thr Val Asp Ser Val Asn Ser Thr Asn Asp Gly Leu Ile Tyr Thr
865 870 875 880

tat gat agt aaa tat ttg cag tca cca aga gta agt gat ttg aaa gat 2688
Tyr Asp Ser Lys Tyr Leu Gln Ser Pro Arg Val Ser Asp Leu Lys Asp
885 890 895

gcc atg tca aca cat agg ggt ata agg tta tct aaa cca aat ttt ggt 2736
Ala Met Ser Thr His Arg Gly Ile Arg Leu Ser Lys Pro Asn Phe Gly
900 905 910

ggt gcc aat gga act gct aat atg acg gat tct gct tct aca tcc aat 2784
Gly Ala Asn Gly Thr Ala Asn Met Thr Asp Ser Ala Ser Thr Ser Asn
915 920 925

gga tct gtg ttg aat aaa aat atg caa act aca gat gtt gat tca att 2832
Gly Ser Val Leu Asn Lys Asn Met Gln Thr Thr Asp Val Asp Ser Ile
930 935 940

tta agt ggt ctt gaa agt gaa gac gaa gct gcg ttt gtt gtt taa 2877
Leu Ser Gly Leu Glu Ser Glu Asp Glu Ala Ala Phe Val Val
945 950 955

<210> 18
<211> 958
<212> PRT
<213> Candida albicans

<400> 18
Met Asn Leu Phe Gln His Lys His Gln Lys Leu Ile Leu Gln Cys Tyr
1 5 10 15

Pro Ala Gly Lys Ala Val Asp Lys Lys Pro Asn Ser Ser Glu Leu Ser
20 25 30

Tyr Leu Leu Tyr Tyr Ala Ser Thr Arg Arg Val Lys Leu Glu Lys Val
35 40 45

Ile Asn Phe Leu Lys Asp Lys Thr His His Asp Val Gly Arg Asn Arg
50 55 60

Thr Gly Asn Leu Gln Val Thr Leu Ala Ile Ile Gln Glu Leu Ile Lys
65 70 75 80

Lys Cys Ser Glu Asn Leu Asn Val Phe Ala Phe Gln Val Cys Tyr Ile
85 90 95

Leu Gln Leu Ile Ala Asn Thr Lys Asp Leu Ala Leu Cys Lys Asn Val
100 105 110

Val Lys Thr Phe Gly Val Leu Cys Glu Asn Leu Asp Gly Gly Leu Phe
115 120 125

Thr Gly Asp Lys Glu Phe Ile Lys Ile Phe Thr Glu Val Phe Gln Thr
130 135 140

Leu Val Ser Phe Gly Lys Asp Arg Ser Gly Val Thr Gln Tyr Asp Trp
145 150 155 160

Gln Met Ile Ser Leu Met Ala Ile Asn Asp Ile Ser Ser Cys Leu Ser
165 170 175

Tyr Asn Ala Ala Val Gly Lys Lys Phe Ile Ala Leu Ser Ile Pro Val
180 185 190

Leu Leu Gln Phe Ile Ile Ala Asn Asn Pro Gln Ser Ser Ile Leu Gln
195 200 205

Arg Leu Lys Ser Asn Leu His Val Glu Asp Asp Gly Lys Arg Leu Ser
210 215 220

Arg Ala His Leu Gln Lys Ser His Ser Lys Ile Ala Gln Gln Ile Asp
225 230 235 240

Asp Asp Phe Thr Asn Asp Ser Leu Thr Leu Thr Asp Ile Thr Glu Lys

245 250 255

Ala Phe Ser Ser Met Lys Ser Phe Phe Asn Thr Asn Ala Ala Ser Gln
260 265 270

Ile Ser Glu Val Thr Arg Ala Val Val Gln His Asn Ile Leu Asn Gly
275 280 285

Thr Asp Leu Glu Trp Gly Val Ser Phe Leu Glu Leu Cys Ile Thr Trp
290 295 300

Ile Pro Val Gln Leu Arg Phe Val Ser Leu Ser Thr Leu Leu Ala Thr
305 310 315 320

Leu Gly Arg Ile Asn Ile Glu Gly Asn Thr Lys Ser Asn Tyr Asn Met
325 330 335

Gln Phe Gln Tyr Ala Arg Tyr Leu Leu Gly Leu Leu Ser Ser Arg Val
340 345 350

Asn Met Ile Gly Leu Ser Val Ser Asp Ile Ile Gln Gln Leu Leu Ser
355 360 365

Leu Gln Ala Asp Leu Ile Leu Lys Ala Ser Asp Leu Asp Lys Ser Glu
370 375 380

Ile Ser Ile Leu Thr Asp Ile Tyr Ser Asp Cys Ile Cys Ser Leu Thr
385 390 395 400

Thr His Ile Tyr Tyr Phe Asp Gln Val Pro Asp Ser Ile Gln Glu Ile
405 410 415

Leu Ile Lys Ile Asp Tyr Ile Leu Glu Ser Ser Phe Val Glu Asp Asn
420 425 430

Asn Ile Thr Ser Thr Gly Glu Gln Ile Gln Asp Leu Ile Ile Gln Leu
435 440 445

Leu Asp Asn Ile Ser Lys Ile Phe Leu Ile Leu Lys Asn Lys Ser Ser
450 455 460

Ser Ile Asn Arg Asn His Val Asn Leu Glu His Trp Asp Ile Ser Leu
465 470 475 480

Gly Leu Leu Ala Pro Gln Gly Asp His Asp Asp Asn Arg Lys Met Ile
485 490 495

Ile Ser Thr Thr Gln Leu Ile Asn Ile Gln Ala Arg Tyr Leu Lys Val
500 505 510

Phe Asp Glu Phe Leu Asn Asn Glu Leu Ala Val Gly Asn Ser Lys Lys
515 520 525

Ser Tyr Asp Leu Leu Ser Lys Gln Ser Arg Leu Asp Pro Gly Ser Thr
530 535 540

Ala Val Glu Gly Val Asn Lys Ser Asp Asp Leu Asp Asn Gly Lys Asp

545 550 555 560

Phe Lys Lys Pro Asp Ala Asn Gln Tyr Ile Thr Asn Gln Gln Asn Phe
565 570 575

Ile Ser His Phe Leu Met Tyr Ile Asp Lys Phe Phe Glu Asn Tyr Asp
580 585 590

Ser Pro Asn Thr Gln Ser Val Leu Leu Leu Val Thr Val Leu Lys Asp
595 600 605

Met Met Asn Ile Leu Gly Leu Asn Phe Leu Ser Asn Phe Ile Pro Phe
610 615 620

Phe His His Trp Val Met Lys Val Asn Arg Ala Ser Asn Phe Thr Gln
625 630 635 640

Arg Gln Lys Phe Lys Asp Thr Phe Ala His Ile Ile Leu Tyr Tyr Met
645 650 655

Leu Lys Asp Leu Asp Glu Gln Tyr Ser His Asp Leu Gln Asn Tyr Cys
660 665 670

Lys Ser Ser Lys Leu Phe Lys Gln Ile Leu Asp Ala Val Glu Tyr Arg
675 680 685

Lys Met Gln Lys Phe Trp Val His Gly Ile Asp Pro Ser Pro Ser Asp
690 695 700

Leu Glu Asn Thr Lys Gly Asp Arg Thr Ile Pro Thr Asp Ala Asn Gly
705 710 715 720

Asn Tyr Ile Ala Ile Arg Ile Lys Pro Glu Asn Ile Glu Glu Phe Ala
725 730 735

Cys Gly Asn Asn Phe Leu Ile Val Trp Leu His Pro Gln Lys Gln Leu
740 745 750

Leu Thr Glu Ile Glu Lys Ser Gln Val Ser Thr His Met Ser Thr Phe
755 760 765

Asn Asn Asp Ser Arg Asn Thr Asn Met Thr Val Ile Met Asp Gln Gly
770 775 780

Ser Leu Ala Leu Ser Gly Gly Ala Asp His Gly Gly His Phe Val Pro
785 790 795 800

Pro Pro Glu Phe Val Asn His Thr Gly Leu Ser Ser Glu Ser Ala Ser
805 810 815

Ser Asn Ser Glu Lys Gly Leu Tyr Thr Gly Leu Gly Leu Gly Thr Ala
820 825 830

Gly Asp Ile Thr Met Ile His Ser Glu Ile Leu Gln Tyr Ser Gln His
835 840 845

Phe Gln Glu Arg Gly Leu Pro His Gly Asn Gly Phe Ala Thr Ile Leu

850 855 860

Arg Thr Val Asp Ser Val Asn Ser Thr Asn Asp Gly Leu Ile Tyr Thr
865 870 875 880

Tyr Asp Ser Lys Tyr Leu Gln Ser Pro Arg Val Ser Asp Leu Lys Asp
885 890 895

Ala Met Ser Thr His Arg Gly Ile Arg Leu Ser Lys Pro Asn Phe Gly
900 905 910

Gly Ala Asn Gly Thr Ala Asn Met Thr Asp Ser Ala Ser Thr Ser Asn
915 920 925

Gly Ser Val Leu Asn Lys Asn Met Gln Thr Thr Asp Val Asp Ser Ile
930 935 940

Leu Ser Gly Leu Glu Ser Glu Asp Glu Ala Ala Phe Val Val
945 950 955

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aaaggcaaaa acattcaagt tttcactaca ttttttgatt aattcctgaa taatggctaa 180

tgtgacttgt aaattaccag tacggtttct accaacatca tgatgagttt tatctttcaa 240

aaaattaatc accttttcta atttgactct acgagtggat gcatagtata ataaataact 300

taactcggac gagttgggtt ttttgtccac tgctttccca gcaggataac attgtaatat 360

taacttttga tgtttatgtt gaaacaaatt cattcttgga tctggaagtt gaagaaacta 420

ttgaatcaaa acaggattta attaaccaat agaaaagaag taactcttga gttaaaaagg 480

atattcttga tgaaaaaaag gagaaaaaag gggaaagaag actctgaaaa tgaattaaag 540

aaacaagaaa aaagtgatca aatgattgaa taaatgaaag taggtaaaaa atga 594

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<223> gene CaDR325

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1 5 10 15

act ttg gat gaa ata aaa tat gcc atg aaa cat gtt ttc caa gat gct 96
Thr Leu Asp Glu Ile Lys Tyr Ala Met Lys His Val Phe Gln Asp Ala
20 25 30

caa tta ggt tta gca gga cat aga aaa tta gtg gta att ttg aaa aat 144
Gln Leu Gly Leu Ala Gly His Arg Lys Leu Val Val Ile Leu Lys Asn
35 40 45

gta ttt aaa aaa gcc att gaa tta aat caa att aat ttc ttt gcc atg 192
Val Phe Lys Lys Ala Ile Glu Leu Asn Gln Ile Asn Phe Phe Ala Met
50 55 60

tgt ttt act aaa ttg tta tct aaa gta tta cct ttg aaa aga gga gtt 240
Cys Phe Thr Lys Leu Leu Ser Lys Val Leu Pro Leu Lys Arg Gly Val
65 70 75 80

ttg gca ggt gat aga ata gtc aaa ttt tgt tat ctg ttt gtt aat ggt 288
Leu Ala Gly Asp Arg Ile Val Lys Phe Cys Tyr Leu Phe Val Asn Gly
85 90 95

ctt gta aaa gat gcc aat gaa gaa aaa cgt tcc aaa gaa gaa gaa aaa 336
Leu Val Lys Asp Ala Asn Glu Glu Lys Arg Ser Lys Glu Glu Glu Lys
100 105 110

gaa gaa aaa gac aaa gac gaa gac aaa gat acg aat gaa agt gat aaa 384
Glu Glu Lys Asp Lys Asp Glu Asp Lys Asp Thr Asn Glu Ser Asp Lys
115 120 125

aat gaa gaa gat cag gaa gat caa gaa gga gaa gga gat caa gaa act 432
Asn Glu Glu Asp Gln Glu Asp Gln Glu Gly Glu Gly Asp Gln Glu Thr
130 135 140

cca att tcg gaa ttc ata tca tat ttg ata aaa tat tta ttg agt ggg 480
Pro Ile Ser Glu Phe Ile Ser Tyr Leu Ile Lys Tyr Leu Leu Ser Gly
145 150 155 160

ata gag gct aaa gat aaa ctg gtt cgt tat cgt gtt gta caa aca tta 528
Ile Glu Ala Lys Asp Lys Leu Val Arg Tyr Arg Val Val Gln Thr Leu
165 170 175

gca tac ttg gtt gaa ttc ttg acc gag ata cac gag aat aat aca ttg 576
Ala Tyr Leu Val Glu Phe Leu Thr Glu Ile His Glu Asn Asn Thr Leu
180 185 190

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gaa gcg tta tat act tta tta agt aat agg cta caa gat aaa gag ctg    624
Glu Ala Leu Tyr Thr Leu Leu Ser Asn Arg Leu Gln Asp Lys Glu Leu
        195                 200                 205

tcg ata cgt att caa gct gtt gtg gca tta tca cat ttt caa tta ttt    672
Ser Ile Arg Ile Gln Ala Val Val Ala Leu Ser His Phe Gln Leu Phe
    210                 215                 220

gaa ttt agt att gaa ggt gat act gga gaa ttt gag gat gaa tta ata    720
Glu Phe Ser Ile Glu Gly Asp Thr Gly Glu Phe Glu Asp Glu Leu Ile
225                 230                 235                 240

tca agt aac caa att cag aat aaa ttg ata aat tcc att caa aat gat    768
Ser Ser Asn Gln Ile Gln Asn Lys Leu Ile Asn Ser Ile Gln Asn Asp
                245                 250                 255

gat agt cca gaa gtc aga cgt gca gca tta atg aat ttg gtt aaa aca    816
Asp Ser Pro Glu Val Arg Arg Ala Ala Leu Met Asn Leu Val Lys Thr
            260                 265                 270

caa gat aca ata ccg att tta ctt gaa cga gcc aga gat tcc aat tct    864
Gln Asp Thr Ile Pro Ile Leu Leu Glu Arg Ala Arg Asp Ser Asn Ser
        275                 280                 285

att aat aga aga ttg gtt tat tct aaa ata gct cgt gaa tta ata act    912
Ile Asn Arg Arg Leu Val Tyr Ser Lys Ile Ala Arg Glu Leu Ile Thr
    290                 295                 300

gat ttg gat gat ctt gaa ttt gaa gat agg gaa ttt tta tta aaa tgg    960
Asp Leu Asp Asp Leu Glu Phe Glu Asp Arg Glu Phe Leu Leu Lys Trp
305                 310                 315                 320

ggg tta aat gat cgt gat gaa act gtt aaa gca gcc gcc act aaa atg    1008
Gly Leu Asn Asp Arg Asp Glu Thr Val Lys Ala Ala Ala Thr Lys Met
                325                 330                 335

ctt acc att tat tgg tat caa tct gtc aat gaa gat tta tta gaa tta    1056
Leu Thr Ile Tyr Trp Tyr Gln Ser Val Asn Glu Asp Leu Leu Glu Leu
            340                 345                 350

att gat caa tta aat gtc aag agt gct ata gct gaa cag gcc ata tta    1104
Ile Asp Gln Leu Asn Val Lys Ser Ala Ile Ala Glu Gln Ala Ile Leu
        355                 360                 365

gca ttt ttt aaa aat aaa cca gaa gtt ctt gaa act att aaa att gat    1152
Ala Phe Phe Lys Asn Lys Pro Glu Val Leu Glu Thr Ile Lys Ile Asp
    370                 375                 380

gaa tca tat tgg aaa aat cta act aca gaa aag gca ttc ttg atg agg    1200
Glu Ser Tyr Trp Lys Asn Leu Thr Thr Glu Lys Ala Phe Leu Met Arg
385                 390                 395                 400

acg ttt tat caa tat tgt aat gag aat caa tta cat gct tta atg gat    1248
Thr Phe Tyr Gln Tyr Cys Asn Glu Asn Gln Leu His Ala Leu Met Asp
                405                 410                 415
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gcc aat ttc cct gaa tta ctt gat ttg tca ata aca tta gaa aag tat 1296
Ala Asn Phe Pro Glu Leu Leu Asp Leu Ser Ile Thr Leu Glu Lys Tyr
420 425 430

ttg tca gtg agg ttg aaa act ata aat gaa aat gaa aat tta gtt aag 1344
Leu Ser Val Arg Leu Lys Thr Ile Asn Glu Asn Glu Asn Leu Val Lys
435 440 445

aca tgg gaa act tat aat gcc aag att gac gaa tta gat gat caa ata 1392
Thr Trp Glu Thr Tyr Asn Ala Lys Ile Asp Glu Leu Asp Asp Gln Ile
450 455 460

ttt agt ctt gaa aac cag att tcc aga ata aat act gat gcc gat aat 1440
Phe Ser Leu Glu Asn Gln Ile Ser Arg Ile Asn Thr Asp Ala Asp Asn
465 470 475 480

ttc cgt aaa agt tta tct aac att gaa gaa gat att att gaa atc aat 1488
Phe Arg Lys Ser Leu Ser Asn Ile Glu Glu Asp Ile Ile Glu Ile Asn
485 490 495

att gct aag gat ttg ttc aaa aag aga att aaa caa ttg aaa aac aac 1536
Ile Ala Lys Asp Leu Phe Lys Lys Arg Ile Lys Gln Leu Lys Asn Asn
500 505 510

agt ggg aat cta gaa gat ttg att act gaa gaa aat caa gag att gct 1584
Ser Gly Asn Leu Glu Asp Leu Ile Thr Glu Glu Asn Gln Glu Ile Ala
515 520 525

gat caa atc aag gat ttc ctg atg gaa gat ttg caa caa caa ttg gaa 1632
Asp Gln Ile Lys Asp Phe Leu Met Glu Asp Leu Gln Gln Gln Leu Glu
530 535 540

gat atc aat aaa aat ctt gat gaa att gaa cat cat cca gaa gat ata 1680
Asp Ile Asn Lys Asn Leu Asp Glu Ile Glu His His Pro Glu Asp Ile
545 550 555 560

acg gct aaa tta gaa gaa ctt caa aca aaa tat gat tct tgt att agg 1728
Thr Ala Lys Leu Glu Glu Leu Gln Thr Lys Tyr Asp Ser Cys Ile Arg
565 570 575

gcg ctt gaa acc act agt gaa ttg aaa att cag act gtt caa atc ttt 1776
Ala Leu Glu Thr Thr Ser Glu Leu Lys Ile Gln Thr Val Gln Ile Phe
580 585 590

gaa caa gaa cat gaa aat gat tgt atc ccc ttt gta gat gct ttg aaa 1824
Glu Gln Glu His Glu Asn Asp Cys Ile Pro Phe Val Asp Ala Leu Lys
595 600 605

gaa tta gaa ttc att att aat caa tta tta tta att gtt aaa gat ttt 1872
Glu Leu Glu Phe Ile Ile Asn Gln Leu Leu Leu Ile Val Lys Asp Phe
610 615 620

gat tat gga gat gaa atg gca aga aga aaa ttg tta cat ata ata aga 1920
Asp Tyr Gly Asp Glu Met Ala Arg Arg Lys Leu Leu His Ile Ile Arg
625 630 635 640

atg aca tta act gaa gat aaa tta cct gat gcg tta ata tca gtg gca 1968

Met Thr Leu Thr Glu Asp Lys Leu Pro Asp Ala Leu Ile Ser Val Ala
645 650 655

ctt aga gta tta cga gca ctt tct ata aat gaa aaa gat ttt gtt tcc 2016
Leu Arg Val Leu Arg Ala Leu Ser Ile Asn Glu Lys Asp Phe Val Ser
660 665 670

atg gcg gta gaa ata att act gat att cgt gat tct cga gat gat gaa 2064
Met Ala Val Glu Ile Ile Thr Asp Ile Arg Asp Ser Arg Asp Asp Glu
675 680 685

gag ttc cat tct gct gcc gct aca ttt gat gat gat gat gat gat att 2112
Glu Phe His Ser Ala Ala Ala Thr Phe Asp Asp Asp Asp Asp Asp Ile
690 695 700

ttg gga aat ggt gat gat gaa tct caa caa tca tca tca ctc agt gca 2160
Leu Gly Asn Gly Asp Asp Glu Ser Gln Gln Ser Ser Ser Leu Ser Ala
705 710 715 720

gta aca aag aag cga aga att gaa cca gat atg cca cca gat gat att 2208
Val Thr Lys Lys Arg Arg Ile Glu Pro Asp Met Pro Pro Asp Asp Ile
725 730 735

gtg tta aga tgt ctt acc atg aca caa tat gta ttg gaa gta att act 2256
Val Leu Arg Cys Leu Thr Met Thr Gln Tyr Val Leu Glu Val Ile Thr
740 745 750

cat agt ttg gat gat cat ctt tca ttg agt tct att tac agt ggt att 2304
His Ser Leu Asp Asp His Leu Ser Leu Ser Ser Ile Tyr Ser Gly Ile
755 760 765

gtc aat tat gct att cag aat gaa tcg aaa aag aaa tta tat ctt gct 2352
Val Asn Tyr Ala Ile Gln Asn Glu Ser Lys Lys Lys Leu Tyr Leu Ala
770 775 780

ggg tta act tgt tta gga ctt tat tct tta att gat tcc aaa att gcc 2400
Gly Leu Thr Cys Leu Gly Leu Tyr Ser Leu Ile Asp Ser Lys Ile Ala
785 790 795 800

aga att gca act aca aca tta tta ctg gca atg aga agt aat ggt gaa 2448
Arg Ile Ala Thr Thr Thr Leu Leu Leu Ala Met Arg Ser Asn Gly Glu
805 810 815

gaa gtg aaa gag att gga atg aaa gct att gtg gat ata ttg gca att 2496
Glu Val Lys Glu Ile Gly Met Lys Ala Ile Val Asp Ile Leu Ala Ile
820 825 830

tat ggt atg agt att ctt gat aaa tca tct aaa tac aaa tat tca aga 2544
Tyr Gly Met Ser Ile Leu Asp Lys Ser Ser Lys Tyr Lys Tyr Ser Arg
835 840 845

atg ttt ttc aaa gtt tta aat tca ttt gat gca cca aaa tta caa tgc 2592
Met Phe Phe Lys Val Leu Asn Ser Phe Asp Ala Pro Lys Leu Gln Cys
850 855 860

att gtc gct gaa gga tta tgc aaa ttg ttt tta gcc gat att ttg tac 2640
Ile Val Ala Glu Gly Leu Cys Lys Leu Phe Leu Ala Asp Ile Leu Tyr

865 870 875 880

aag act gac aaa cgg agt tta ttt gga aat gct att caa ggt ggt ggt 2688
Lys Thr Asp Lys Arg Ser Leu Phe Gly Asn Ala Ile Gln Gly Gly Gly
885 890 895

ggt ggt ggt ggt ggt aat gat gat cca act acc acc aat gac gat gaa 2736
Gly Gly Gly Gly Gly Asn Asp Asp Pro Thr Thr Thr Asn Asp Asp Glu
900 905 910

act gaa gaa gaa aca gat cga gag cat gaa aag cat tta ttt gaa gcg 2784
Thr Glu Glu Glu Thr Asp Arg Glu His Glu Lys His Leu Phe Glu Ala
915 920 925

att gta ctt att tat ttc aac ccc aac acc aaa tca aat caa gaa tta 2832
Ile Val Leu Ile Tyr Phe Asn Pro Asn Thr Lys Ser Asn Gln Glu Leu
930 935 940

caa caa att ttg tca ttt tgt att cca gtt tat gcc ttt tct cat ata 2880
Gln Gln Ile Leu Ser Phe Cys Ile Pro Val Tyr Ala Phe Ser His Ile
945 950 955 960

aat cat caa atc aat tta gct gca gtt agt ggt gat gtt att tat cga 2928
Asn His Gln Ile Asn Leu Ala Ala Val Ser Gly Asp Val Ile Tyr Arg
965 970 975

ctt ttc act gaa aca gaa aca gaa tta tca cca agt gtt ata atc cct 2976
Leu Phe Thr Glu Thr Glu Thr Glu Leu Ser Pro Ser Val Ile Ile Pro
980 985 990

caa tta ata tca tgg tgt gat cct cga aat tta gtt aaa tta tcg aat 3024
Gln Leu Ile Ser Trp Cys Asp Pro Arg Asn Leu Val Lys Leu Ser Asn
995 1000 1005

gag gaa ata aat caa gca aca tca cat tta tgg caa tgt gtt tat tta 3072
Glu Glu Ile Asn Gln Ala Thr Ser His Leu Trp Gln Cys Val Tyr Leu
1010 1015 1020

tta caa gtg gtt gaa caa gta gat gct cgt aat gtt aaa aga tgc atc 3120
Leu Gln Val Val Glu Gln Val Asp Ala Arg Asn Val Lys Arg Cys Ile
1025 1030 1035 1040

att aac aat ttg aat aaa ttt cat ata acg gaa gaa tta gag tca aat 3168
Ile Asn Asn Leu Asn Lys Phe His Ile Thr Glu Glu Leu Glu Ser Asn
1045 1050 1055

caa tta caa gct tta att aaa gct ctt gat gct aca gtt gaa tta ttt 3216
Gln Leu Gln Ala Leu Ile Lys Ala Leu Asp Ala Thr Val Glu Leu Phe
1060 1065 1070

act aat aat gaa gat aac cct aat ttt atc ttg gat aaa cca aca aag 3264
Thr Asn Asn Glu Asp Asn Pro Asn Phe Ile Leu Asp Lys Pro Thr Lys
1075 1080 1085

aag aat ttt gat act ttt att gaa tca ata aag aat aaa ttg gaa att 3312
Lys Asn Phe Asp Thr Phe Ile Glu Ser Ile Lys Asn Lys Leu Glu Ile
1090 1095 1100

gct caa aaa aga gaa gaa aat gaa ctg att aaa agt ggt aca aat tca 3360
Ala Gln Lys Arg Glu Glu Asn Glu Leu Ile Lys Ser Gly Thr Asn Ser
1105 1110 1115 1120

ata tta cat gaa tta gat gat tta gat att gga act gga gag agt agt 3408
Ile Leu His Glu Leu Asp Asp Leu Asp Ile Gly Thr Gly Glu Ser Ser
1125 1130 1135

caa ata tct ata aaa tca gaa aca aaa aga aga gat ctg gat cga tct 3456
Gln Ile Ser Ile Lys Ser Glu Thr Lys Arg Arg Asp Leu Asp Arg Ser
1140 1145 1150

ctg caa gtt agt aaa act acg tca cca gaa act tca gaa aat gaa gat 3504
Leu Gln Val Ser Lys Thr Thr Ser Pro Glu Thr Ser Glu Asn Glu Asp
1155 1160 1165

gaa gag gat gat aat gag gag gag gaa caa gag aag aag aaa agt ttt 3552
Glu Glu Asp Asp Asn Glu Glu Glu Glu Gln Glu Lys Lys Lys Ser Phe
1170 1175 1180

act gat gga aaa aat aaa ctt gaa cta aag gca gat aag cca atc aca 3600
Thr Asp Gly Lys Asn Lys Leu Glu Leu Lys Ala Asp Lys Pro Ile Thr
1185 1190 1195 1200

ttt aaa gct gaa gac aag agg gaa ggg tca gtt gaa aca gat cat ggt 3648
Phe Lys Ala Glu Asp Lys Arg Glu Gly Ser Val Glu Thr Asp His Gly
1205 1210 1215

caa gaa caa gtt cta gtt gaa tca aag aaa gtc att gat agt aat gtt 3696
Gln Glu Gln Val Leu Val Glu Ser Lys Lys Val Ile Asp Ser Asn Val
1220 1225 1230

gaa gat tct tta gaa gat ata gat aag ttt tta gaa gaa gca gat gat 3744
Glu Asp Ser Leu Glu Asp Ile Asp Lys Phe Leu Glu Glu Ala Asp Asp
1235 1240 1245

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1250 1255

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Gln Leu Gly Leu Ala Gly His Arg Lys Leu Val Val Ile Leu Lys Asn
35 40 45

Val Phe Lys Lys Ala Ile Glu Leu Asn Gln Ile Asn Phe Phe Ala Met
50 55 60

Cys Phe Thr Lys Leu Leu Ser Lys Val Leu Pro Leu Lys Arg Gly Val
65 70 75 80

Leu Ala Gly Asp Arg Ile Val Lys Phe Cys Tyr Leu Phe Val Asn Gly
85 90 95

Leu Val Lys Asp Ala Asn Glu Glu Lys Arg Ser Lys Glu Glu Glu Lys
100 105 110

Glu Glu Lys Asp Lys Asp Glu Asp Lys Asp Thr Asn Glu Ser Asp Lys
115 120 125

Asn Glu Glu Asp Gln Glu Asp Gln Glu Gly Glu Gly Asp Gln Glu Thr
130 135 140

Pro Ile Ser Glu Phe Ile Ser Tyr Leu Ile Lys Tyr Leu Leu Ser Gly
145 150 155 160

Ile Glu Ala Lys Asp Lys Leu Val Arg Tyr Arg Val Val Gln Thr Leu
165 170 175

Ala Tyr Leu Val Glu Phe Leu Thr Glu Ile His Glu Asn Asn Thr Leu
180 185 190

Glu Ala Leu Tyr Thr Leu Leu Ser Asn Arg Leu Gln Asp Lys Glu Leu
195 200 205

Ser Ile Arg Ile Gln Ala Val Val Ala Leu Ser His Phe Gln Leu Phe
210 215 220

Glu Phe Ser Ile Glu Gly Asp Thr Gly Glu Phe Glu Asp Glu Leu Ile
225 230 235 240

Ser Ser Asn Gln Ile Gln Asn Lys Leu Ile Asn Ser Ile Gln Asn Asp
245 250 255

Asp Ser Pro Glu Val Arg Arg Ala Ala Leu Met Asn Leu Val Lys Thr
260 265 270

Gln Asp Thr Ile Pro Ile Leu Leu Glu Arg Ala Arg Asp Ser Asn Ser
275 280 285

Ile Asn Arg Arg Leu Val Tyr Ser Lys Ile Ala Arg Glu Leu Ile Thr
290 295 300

Asp Leu Asp Asp Leu Glu Phe Glu Asp Arg Glu Phe Leu Leu Lys Trp
305 310 315 320

Gly Leu Asn Asp Arg Asp Glu Thr Val Lys Ala Ala Ala Thr Lys Met
325 330 335

Leu Thr Ile Tyr Trp Tyr Gln Ser Val Asn Glu Asp Leu Leu Glu Leu
340 345 350

Ile Asp Gln Leu Asn Val Lys Ser Ala Ile Ala Glu Gln Ala Ile Leu
355 360 365

Ala Phe Phe Lys Asn Lys Pro Glu Val Leu Glu Thr Ile Lys Ile Asp
370 375 380

Glu Ser Tyr Trp Lys Asn Leu Thr Thr Glu Lys Ala Phe Leu Met Arg
385 390 395 400

Thr Phe Tyr Gln Tyr Cys Asn Glu Asn Gln Leu His Ala Leu Met Asp
405 410 415

Ala Asn Phe Pro Glu Leu Leu Asp Leu Ser Ile Thr Leu Glu Lys Tyr
420 425 430

Leu Ser Val Arg Leu Lys Thr Ile Asn Glu Asn Glu Asn Leu Val Lys
435 440 445

Thr Trp Glu Thr Tyr Asn Ala Lys Ile Asp Glu Leu Asp Asp Gln Ile
450 455 460

Phe Ser Leu Glu Asn Gln Ile Ser Arg Ile Asn Thr Asp Ala Asp Asn
465 470 475 480

Phe Arg Lys Ser Leu Ser Asn Ile Glu Glu Asp Ile Ile Glu Ile Asn
485 490 495

Ile Ala Lys Asp Leu Phe Lys Lys Arg Ile Lys Gln Leu Lys Asn Asn
500 505 510

Ser Gly Asn Leu Glu Asp Leu Ile Thr Glu Glu Asn Gln Glu Ile Ala
515 520 525

Asp Gln Ile Lys Asp Phe Leu Met Glu Asp Leu Gln Gln Gln Leu Glu
530 535 540

Asp Ile Asn Lys Asn Leu Asp Glu Ile Glu His His Pro Glu Asp Ile
545 550 555 560

Thr Ala Lys Leu Glu Glu Leu Gln Thr Lys Tyr Asp Ser Cys Ile Arg
565 570 575

Ala Leu Glu Thr Thr Ser Glu Leu Lys Ile Gln Thr Val Gln Ile Phe
580 585 590

Glu Gln Glu His Glu Asn Asp Cys Ile Pro Phe Val Asp Ala Leu Lys
595 600 605

Glu Leu Glu Phe Ile Ile Asn Gln Leu Leu Leu Ile Val Lys Asp Phe
610 615 620

Asp Tyr Gly Asp Glu Met Ala Arg Arg Lys Leu Leu His Ile Ile Arg
625 630 635 640

Met Thr Leu Thr Glu Asp Lys Leu Pro Asp Ala Leu Ile Ser Val Ala
645 650 655

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Leu Arg Val Leu Arg Ala Leu Ser Ile Asn Glu Lys Asp Phe Val Ser
            660                 665                 670

Met Ala Val Glu Ile Ile Thr Asp Ile Arg Asp Ser Arg Asp Asp Glu
        675                 680                 685

Glu Phe His Ser Ala Ala Ala Thr Phe Asp Asp Asp Asp Asp Asp Ile
    690                 695                 700

Leu Gly Asn Gly Asp Asp Glu Ser Gln Gln Ser Ser Ser Leu Ser Ala
705                 710                 715                     720

Val Thr Lys Lys Arg Arg Ile Glu Pro Asp Met Pro Pro Asp Asp Ile
                725                 730                 735

Val Leu Arg Cys Leu Thr Met Thr Gln Tyr Val Leu Glu Val Ile Thr
            740                 745                 750

His Ser Leu Asp Asp His Leu Ser Leu Ser Ser Ile Tyr Ser Gly Ile
        755                 760                 765

Val Asn Tyr Ala Ile Gln Asn Glu Ser Lys Lys Lys Leu Tyr Leu Ala
    770                 775                 780

Gly Leu Thr Cys Leu Gly Leu Tyr Ser Leu Ile Asp Ser Lys Ile Ala
785                 790                 795                     800

Arg Ile Ala Thr Thr Thr Leu Leu Leu Ala Met Arg Ser Asn Gly Glu
                805                 810                 815

Glu Val Lys Glu Ile Gly Met Lys Ala Ile Val Asp Ile Leu Ala Ile
            820                 825                 830

Tyr Gly Met Ser Ile Leu Asp Lys Ser Ser Lys Tyr Lys Tyr Ser Arg
        835                 840                 845

Met Phe Phe Lys Val Leu Asn Ser Phe Asp Ala Pro Lys Leu Gln Cys
    850                 855                 860

Ile Val Ala Glu Gly Leu Cys Lys Leu Phe Leu Ala Asp Ile Leu Tyr
865                 870                 875                     880

Lys Thr Asp Lys Arg Ser Leu Phe Gly Asn Ala Ile Gln Gly Gly Gly
                885                 890                 895

Gly Gly Gly Gly Gly Asn Asp Asp Pro Thr Thr Thr Asn Asp Asp Glu
            900                 905                 910

Thr Glu Glu Glu Thr Asp Arg Glu His Glu Lys His Leu Phe Glu Ala
        915                 920                 925

Ile Val Leu Ile Tyr Phe Asn Pro Asn Thr Lys Ser Asn Gln Glu Leu
    930                 935                 940

Gln Gln Ile Leu Ser Phe Cys Ile Pro Val Tyr Ala Phe Ser His Ile
945                 950                 955                     960
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Asn His Gln Ile Asn Leu Ala Ala Val Ser Gly Asp Val Ile Tyr Arg
965 970 975

Leu Phe Thr Glu Thr Glu Thr Glu Leu Ser Pro Ser Val Ile Ile Pro
980 985 990

Gln Leu Ile Ser Trp Cys Asp Pro Arg Asn Leu Val Lys Leu Ser Asn
995 1000 1005

Glu Glu Ile Asn Gln Ala Thr Ser His Leu Trp Gln Cys Val Tyr Leu
1010 1015 1020

Leu Gln Val Val Glu Gln Val Asp Ala Arg Asn Val Lys Arg Cys Ile
025 1030 1035 1040

Ile Asn Asn Leu Asn Lys Phe His Ile Thr Glu Glu Leu Glu Ser Asn
1045 1050 1055

Gln Leu Gln Ala Leu Ile Lys Ala Leu Asp Ala Thr Val Glu Leu Phe
1060 1065 1070

Thr Asn Asn Glu Asp Asn Pro Asn Phe Ile Leu Asp Lys Pro Thr Lys
1075 1080 1085

Lys Asn Phe Asp Thr Phe Ile Glu Ser Ile Lys Asn Lys Leu Glu Ile
1090 1095 1100

Ala Gln Lys Arg Glu Glu Asn Glu Leu Ile Lys Ser Gly Thr Asn Ser
105 1110 1115 1120

Ile Leu His Glu Leu Asp Asp Leu Asp Ile Gly Thr Gly Glu Ser Ser
1125 1130 1135

Gln Ile Ser Ile Lys Ser Glu Thr Lys Arg Arg Asp Leu Asp Arg Ser
1140 1145 1150

Leu Gln Val Ser Lys Thr Thr Ser Pro Glu Thr Ser Glu Asn Glu Asp
1155 1160 1165

Glu Glu Asp Asp Asn Glu Glu Glu Glu Gln Glu Lys Lys Lys Ser Phe
1170 1175 1180

Thr Asp Gly Lys Asn Lys Leu Glu Leu Lys Ala Asp Lys Pro Ile Thr
185 1190 1195 1200

Phe Lys Ala Glu Asp Lys Arg Glu Gly Ser Val Glu Thr Asp His Gly
1205 1210 1215

Gln Glu Gln Val Leu Val Glu Ser Lys Lys Val Ile Asp Ser Asn Val
1220 1225 1230

Glu Asp Ser Leu Glu Asp Ile Asp Lys Phe Leu Glu Glu Ala Asp Asp
1235 1240 1245

Val Asp Tyr Gly Asp Ile Ser Met Asp
1250 1255

<210> 22
<211> 603
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Homologous
Fragment to Sc YDR325

<400> 22
ctgtttgtta atggtcttgt aaaagatgcc aatgaagaaa aacgttccaa agaagaagaa 60

aaagaagaga aagacaaaga caaagacaaa gatacgaatg aaagtgataa aaatgaagaa 120

gatcaggaag atcaagaagg agaaggagat caagaaactc caatttcgga attcatatca 180

tatttgataa aatatttatt gagtgggata gaggctaaag ataaactggt tcgttatcgt 240

gttgtacaaa cattagcata cttggttgaa ttcttgaccg agatacacga gaataataca 300

ttggaagcgt tatatacttt attaagtaat aggctacaag ataaagagct gtcgatacgt 360

attcaagctg ttgtggcatt atcacatttt caattatttg aatttagtat tgaaggtgat 420

actggagaat ttgaggatga attaatatca agtaaccaaa ttcagaataa attgataaat 480

tccattcaaa atgatgatag tccagaagtc agacgtgcag cattaatgaa tttggttaaa 540

acacaagata caataccgat tttacttgag cgagccagag attccaattc tattaataga 600

aga 603

<210> 23
<211> 581
<212> DNA
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<220>
<223> Description of Artificial Sequence: Homologous
Fragment to Sc YDR325

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ttggtatcaa tctgtcaatg aagatttatt agaattaatt gatcaattaa atgtcagaag 120

tgctatagct gaacaggcca tattagcatt ttttaaaaat aaaccagaag ttcttgcaac 180

tattaaaatt gatgaatcat attggaaaaa tctaactaca gaaaaggcat tcttgatgag 240

gacgttttat caatattgta atgagaatca attacatgct ttaatggatg ccaatttccc 300

tgaattactt gatttgtcaa taacattaga aaagtatttg tcagtgaggt tgaaaacaat 360

aaatgaaaat gaaaatttaa ttaagacatg ggaaacttat aatgccaaga ttgacgaatt 420

agatgatcaa atatttagtc ttgaaaacca gatttccaga ataaatactg atgccgataa 480

tttccgtaaa agtttatcta acattgaaga agatattatt gaaatcaata ttgctaagga 540

tttgttcaaa aagagaatta aacaattgaa aaactgagca c 581

<210> 24
<211> 662
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Homologous
Fragment to Sc YDR325

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attcaaggtg gtggtggtgg tgatgatcca actaccacca atgacgatga aactgaagaa 180

gaaacagatc gagagcatga aaagcattta tttgaagcga ttgtacttat ttatttcaac 240

cccaacacca aatcaaatca agaattacaa caaattttgt cattttgtat tccagtttat 300

gccttttctc atataaatca tcaaatcaat ttagctgcag ttagtggtga tgttatttat 360

cgacttttca ctgaaacaga aacagaatta tcaccaagtg ttataatccc tcaattaata 420

tcatggtgtg atcctcgaaa tttagttaaa ttatcgaatg aggaaataaa tcaagcaaca 480

tcacatttat ggcaatgtgt ttatttatta caagtggttg aacaagtaga tgctcgtaat 540

gttaaaagat gcatcattaa caatttgaat aaatttcata taacggaaga attagaatca 600

aatcaattac aagctttaat taaagctctt gatgctacag ttgaattatt tactaataat 660

ga 662

<210> 25
<211> 231
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Homologous
Fragment to Sc YOR110

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gttaaaatca gttactgatg ttatagatga taatcaaact gtgttacgtg ctggtgcatg 120

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ttcattatcc aaatttgtta gagatggcga agataaaacc aatcatacta ttcaatggaa 180

aattgtcatg aatggtaatt gtgaattctt gacacagggt gaagaaatga a          231


 aaa gag att gga atg aaa gct att gtg gat ata ttg gca att   2496
Glu Val Lys Glu Ile Gly Met Lys Ala Ile Val Asp Ile Leu Ala Ile
            820                 825                 830

tat ggt atg agt att ctt gat aaa tca tct aaa tac aaa tat tca aga    2544
Tyr Gly Met Ser Ile Leu Asp Lys Ser Ser Lys Tyr Lys Tyr Ser Arg
        835                 840                 845

atg ttt ttc aaa gtt tta aat tca ttt gat gca cca aaa tta caa tgc    2592
Met Phe Phe Lys Val Leu Asn Ser Phe Asp Ala Pro Lys Leu Gln Cys
    850                 855                 860

att gtc gct gaa gga tta tgc aaa ttg ttt tta gcc gat att ttg tac    2640
Ile Val Ala Glu Gly Leu Cys Lys Leu Phe Leu Ala Asp Ile Leu Tyr
865                 870                 875                 880

aag act gac aaa cgg agt tta ttt gga aat gct att caa ggt ggt ggt    2688
Lys Thr Asp Lys Arg Ser Leu Phe Gly Asn Ala Ile Gln Gly Gly Gly
                885                 890                 895

ggt ggt ggt ggt ggt aat gat gat cca act acc acc aat gac gat gaa    2736
Gly Gly Gly Gly Gly Asn Asp Asp Pro Thr Thr Thr Asn Asp Asp Glu
            900                 905                 910

act gaa gaa gaa aca gat cga gag cat gaa aag cat tta ttt gaa gcg    2784
Thr Glu Glu Glu Thr Asp Arg Glu His Glu Lys His Leu Phe Glu Ala
        915                 920                 925

att gta ctt att tat ttc aac ccc aac acc aaa tca aat caa gaa tta    2832
Ile Val Leu Ile Tyr Phe Asn Pro Asn Thr Lys Ser Asn Gln Glu Leu
    930                 935                 940

caa caa att ttg tca ttt tgt att cca gtt tat gcc ttt tct cat ata    2880
Gln Gln Ile Leu Ser Phe Cys Ile Pro Val Tyr Ala Phe Ser His Ile
945                 950                 955                 960

aat cat caa atc aat tta gct gca gtt agt ggt gat gtt att tat cga    2928
Asn His Gln Ile Asn Leu Ala Ala Val Ser Gly Asp Val Ile Tyr Arg
                965                 970                 975

ctt ttc act gaa aca gaa aca gaa tta tca cca agt gtt ata atc cct    2976
Leu Phe Thr Glu Thr Glu Thr Glu Leu Ser Pro Ser Val Ile Ile Pro
            980                 985                 990

caa tta ata tca tgg tgt gat cct cga aat tta gtt aaa tta tcg aat    3024
Gln Leu Ile Ser Trp Cys Asp Pro Arg Asn Leu Val Lys Leu Ser Asn
        995                 1000                1005

gag gaa ata aat caa gca aca tca cat tta tgg caa tgt gtt tat tta    3072
Glu Glu Ile Asn Gln Ala Thr Ser His Leu Trp Gln Cys Val Tyr Leu
    1010                1015                1020
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tta caa gtg gtt gaa caa gta gat gct cgt aat gtt aaa aga tgc atc    3120
Leu Gln Val Val Glu Gln Val Asp Ala Arg Asn Val Lys Arg Cys Ile
1025                1030                1035                1040

att aac aat ttg a
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